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SIGNIFICANCE OF THE TONSILS IN THE DEVELOPMENT OF THE CHILD

CHAIRMAN'S ADDRESS

ALBERT D. KAISER, M.D.

ROCHESTER, N. Y.

During the last thirty years many significant facts have been ascertained relative to the growth and to the development of the child. Particular attention has been given to the status of the tonsils and adenoids as one of the factors that may influence the child's physical progress. In this period an increasing number of children have been classified as possessing hypertrophied or diseased tonsils resulting in the surgical treatment of the tonsils in nearly 50 per cent of urban children in the United States and England. This situation invites a survey of the tonsil problem and an evaluation of the tonsils as a factor in the child's development.

It is of interest to note that in 1888 W. Franklin Chappell [5] surveyed 2,000 children in New York to determine the frequency of certain abnormal conditions of the tonsils. He concluded that 3 per cent of the children had tonsils sufficiently enlarged to require surgical treatment. Twenty years later Gibb [6] reported on a group of boys at Girard College in Philadelphia and stated that 30 per cent were found to have either hypertrophied tonsils or adenoids or both. During the last twenty years more than 50 per cent of the children in many cities of the United States have been designated as having either hypertrophied or diseased tonsils which necessitated their removal. It is obvious, therefore, that either the lymphoid tissue of the child's nasopharynx has assumed a more formidable position in the throat or the standards for judging the significance of the tonsils have changed. It seems quite unlikely that the tonsils are more frequently hypertrophied today than they were forty years ago. With the lessened morbidity from such diseases as diphtheria and scarlet fever, considered potent factors in producing hypertrophy of the tonsils, one would expect to find fewer children with hypertrophied tonsils. This intensified interest in the tonsils, and the subsequent surgical treatment must be explained by the changed attitude toward the tonsils. In fact the real issue in the discussion dealing with the tonsil problem is to decide whether the widespread incrimination of the tonsils is scientifically sound and if it is in the interest of the child's health. Whatever influences may have been responsible for bringing about the present attitude toward the tonsils and adenoids, it must be recognized that surgery of the tonsils has been widely accepted as both a therapeutic and a prophylactic procedure. The beneficial results following tonsillectomy in selected cases cannot be refuted. When, however, this procedure is applied to half of the children during their school years, it is reasonable to question whether the tonsils can be incriminated in such a high percentage of children and whether the surgical treatment of the tonsils in these children contributes anything to their health.

THE TONSIL PROBLEM TODAY

The problem that confronts the physician today is When should the tonsils be considered a menace to a child's development? There is no dispute as to the surgical procedure when once this decision is made. In obvious cases of hypertrophy and infection of the tonsils the clinical signs are sufficient to direct the course the physician must take. However, in many of the children subjected to surgical treatment of the tonsils in recent years the clinical evidence for tonsillectomy was not clear, for it was not certain that the suspected tonsils were influencing the child's health favorably or unfavorably. For years physiologists have assigned various functions to the tonsils which have not been uniformly accepted. Bacteriologists have reported on the bacterial flora found in the tonsils either from culture or from a study of the tonsils after their removal, but these studies give no substantial aid to the clinician in the problem of deciding whether the tonsils in a given case are a menace to the child's health. As no laboratory test is available to determine whether the tonsils are beneficial or harmful to the child, the clinician's decision must rest on his own experience, on his estimate of all the factors that contribute to the child's well being and on the statistical experience of others. Though one would like to apply rigid scientific standards for evaluating the significance of the tonsils in the development of the child, it is quite obvious that such standards are not known and one must resort to clinical investigations. In approaching the clinical study of this problem one encounters numerous pitfalls which make one wonder whether the clinical and statistical studies recorded present the true picture of the tonsil problem. Selkirk and Mitchell [7] have pointed out that it is difficult to evaluate results in tonsillectomized children because of the variables that exist. The numerous surveys that have been made are based on the accumulation of data which are not obtained by the same methods, so that one must question the real value of such conclusions. When separate and intensive studies of a single symptom in relation to tonsillectomy have

Read before the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the author's reprints.

5. Chappell, W. F.: Am. J. M. Sc. **97**: 148, 1889.

6. Gibb, J. S.: Tr. Am. Laryng. A., 1909.

7. Selkirk, T. K., and Mitchell, A. C.: Evaluation of the Results of Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **42**: 9-41 (July) 1931.

been made, more reliable results have been obtained. Whatever clinical methods are employed, it is essential that control studies should be made simultaneously with those whose tonsils have been removed. For a fair comparison, similar age groups must be utilized and uniformity in the method of examination and follow-up

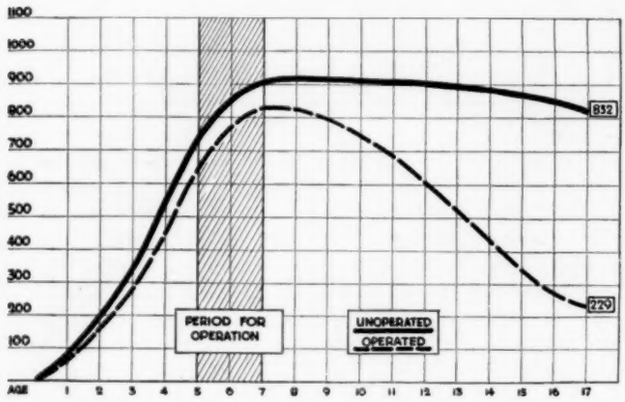

Chart 1.—Tonsillitis and sore throat among 2,200 tonsillectomized and 2,200 nontonsillectomized children.

must be observed in the two groups. Recognizing the difficulties in obtaining genuine control material, it is still possible to get a fair opinion as to the trend of the child's reaction to certain symptoms. Utilizing Yule's formula for determining whether the variation in the trends is significant or not offers some help in evaluating the significance of the tonsils with reference to certain pathologic conditions.

It is generally accepted by physiologists and by clinicians that normal and uninterrupted growth and development in a child requires a sound body at birth. Adequate food intake fortified with the necessary minerals and vitamins is essential during the first few years of life. Acute and chronic infections are known to halt or to retard the development of the child. To minimize the number and the severity of the infections in infants and in young children, specific protective vaccinations are given. Other precautions in protecting the child against infection are taken that might be termed social or environmental. Severe or repeated infections in the nasopharynx and adjoining organs are known to interefere with the uninterrupted development of the child. It therefore seems logical to improve, if possible, the zone in which the infections usually originate. The tonsils and adenoids are not only in this zone of frequent infection but are frequently the victims when pathogenic organisms gain entrance into the nasopharynx. Sufficient clinical evidence is available to show that the tonsils may impede the development of a child either through hypertrophy or as a reservoir of infection. Experience again and again has shown that enucleation of such tonsils removes the focus of infection and permits the growth and the developmental process to proceed without further handicap. In such instances it seems quite certain that the tonsils were a liability to the child and their removal was highly desirable. Can one, however, deduce from these occasional cases that normal tonsils encourage infections of the throat and therefore share with the infections themselves a deterring influence on the child's development? Again mindful of the fact that no convincing scientific evidence is at hand to explain the part the tonsillar tissue plays in the economy of the child, it becomes necessary to follow the development of a group of children to adolescence, recording the sequence and the number of their respiratory infections over a period of years. If the expected development in the group in which the tonsils were removed follows a trend significantly different from the group in which the tonsils were not removed, it might be assumed that the presence or the absence of the tonsils has some influence on the physical development of the child. Such studies have been undertaken to determine whether certain infections are lessened by the removal of the tonsils. With no true normal group available, my associates and I endeavored to compare children of like age and environment whose tonsils were removed with a similar group that presented the same indications for their removal but on whom no operation was performed.

THE PRESENT STUDY

Consideration has been given to the common infections of the upper respiratory tract, tonsillitis, the common cold, otitis media and cervical adenitis. The pulmonary infections bronchitis and pneumonia have been investigated and the various manifestations of rheumatic infection have been recorded. Several reports have been made on a large series of children and on control groups in which these various complaints have been followed for a period of ten years.[8] From these studies it is noted that tonsillitis is a common complaint in young children. Approximately 38 per cent of the 4,400 children utilized in the study were subject to repeated attacks of tonsillitis (at least two febrile attacks a year) during the first seven years of life. Tonsillectomy was advised for all 4,400 children for various reasons but only half of the group submitted, and none of the children in the control group of 2,200 children were operated on during the succeeding years. As is indicated in chart 1, the incidence of sore throat was decidedly lessened during the first three years following the operation and then increased somewhat during the next seven years, but the trend was decidedly downward. In the group in which the operation was not done attacks of tonsillitis recurred with only a slight decrease in frequency during the same years in which the children who were operated on showed a

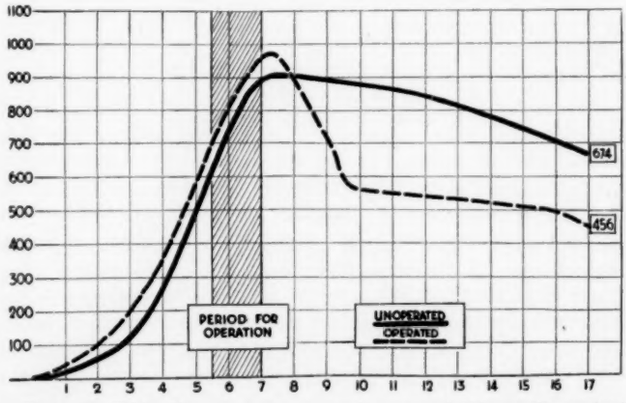

Chart 2.—Colds (four or more a year) among 2,200 tonsillectomized and 2,200 nontonsillectomized children.

lessened incidence. When one compares the incidence of this infection in the two groups it is obvious that the common ailment termed tonsillitis or sore throat occurred less frequently in the cases in which the tonsils had been removed. In other studies, notably those of Selkirk and Mitchell,[7] similar results were obtained as far as this complaint was concerned.

8. Kaiser, A. D.: The Relation of Tonsils and Adenoids to Infections in Children, Am. J. Dis. Child. **41**: 568-581 (March) 1931.

The common cold with its unpleasant complications has frequently influenced physicians and parents to remove the child's tonsils and adenoids, hoping that fewer colds will develop following the operation. It was noted that the incidence of head colds (chart 2, four colds or more a year) occurred with about

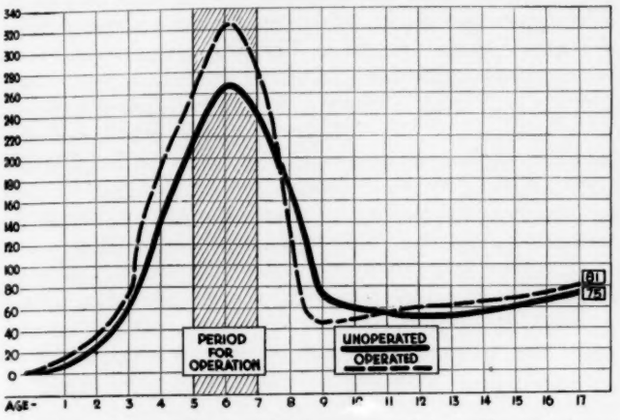

Chart 3.—Otitis media (purulent) among 2,200 tonsillectomized and 2,200 nontonsillectomized children.

equal frequency in the two groups under observation. Approximately 42 per cent of the children were subject to this repeated infection up to the age of 7 years. Following the operation for a period of three years the surgically treated children enjoyed greater freedom from colds than those who did not receive surgical treatment. During the next seven years of observation the children who were operated on actually had more colds than the group who were not. Considering the entire ten year period it must be concluded that the children who were operated on showed only a slight advantage over the children who were not, an advantage which cannot be considered statistically significant. It is quite likely that removal of the adenoids benefited the younger children but as the children advanced in years the adenoid tissue retrograded, so that the children who were not operated on were likewise benefited. Though the trend as far as frequent colds are concerned is downward as the child grows older, there is insufficient evidence to show that the removal of the tonsils is solely responsible for this decline in incidence.

Utilizing the same group for the effect of tonsil and adenoid removal on the incidence of purulent otitis media, we noted that 15 per cent of the children who were subsequently operated on had suffered from purulent otitis media before the ages of from 5 to 7 years, while in the control group 12 per cent were likewise affected. During the three year period following tonsillectomy nearly twice as many children who were not operated on had purulent ear infections, but during the next seven years these children fared as well as and even a little better than those who were operated on. It seems quite certain that ear infections are somewhat influenced by age, for regardless of the presence or absence of the tonsils this type of infection becomes less frequent after the eighth year of life. Again it seems probable that the removal of the adenoids was of distinct benefit to the younger children who were subject to ear infections. Once a middle ear infection is established it is as likely to lead to an infection in the mastoid in tonsillectomized children as in those whose tonsils and adenoids have not been removed. Undoubtedly catarrhal otitis media that leads to impaired hearing is frequently relieved by adenoidectomy in early childhood, but from a study of this group, as chart 3 indicates, the tonsils have no constant relation to infections in the ear.

Cervical adenitis is a common infection in childhood. In each group of this study 15 per cent of the children had definite enlargement of the cervical glands before the ages of 5 and 7 years. Only children in whom there was a visible enlargement of the cervical glands have been considered. In some children this evidence of infection was acute, while in others the enlargement lasted for weeks or for months. During the three year period following tonsillectomy the incidence of cervical adenitis in the children who were operated on was 5 per cent as compared to an incidence of 14 per cent in the children who were not. Over a longer period of time a number of the tonsillectomized children showed a recurrence of cervical adenitis, accounting for an incidence of 7 per cent at the end of ten years, while among the children used as controls the incidence of this complaint was 14 per cent. The statistical evidence in this study as well as in other reported studies shows a significant favorable trend for the relief of this complaint in the groups in which a tonsillectomy had been done.

Though the presence or the repeated occurrence of infections of the upper respiratory tract in children serves as the most common indication for the removal of the tonsils, the subsequent incidence of pulmonary infections must be considered. Pulmonary infections occurred more frequently in children in the first five years of life than in the next ten years. Such is the usual incidence of these infections. Undoubtedly in our groups some children subject to pulmonary infections were operated on because of this tendency, for more of the children who underwent the operation had repeated attacks of bronchitis and pneumonia before the ages of 5 to 7 years than in the group of children who were never operated on. In spite of this, the trend was definitely for more pulmonary infections in the tonsillectomized group over the ten year period than for the control children. It seems that the absence of the tonsils either increased the chances of developing bronchitis

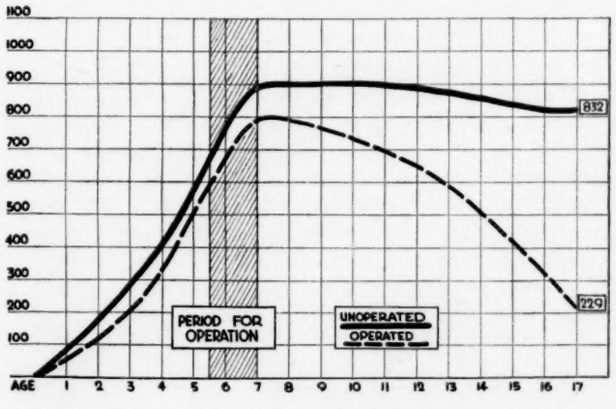

Chart 4.—Cervical adenitis (acute and chronic) among 2,200 tonsillectomized and 2,200 nontonsillectomized children.

and pneumonia or else the tonsillectomized group represented the more susceptible individuals and the operation was not responsible for the increased incidence of pulmonary infections.

Chronic or recurrent diseases such as tuberculosis, asthma, nephritis, diabetes and rheumatic fever are known to influence the development of the child. In the prevention or the control of these diseases the role of the tonsils must be considered.

Statistical studies have been made on 500 children from 5 to 14 years of age in whom positive signs of tuberculosis existed. All the children gave a positive reaction to the intradermal tuberculin test and showed roentgenologic evidence of tuberculosis. An analysis of this group with reference to the presence or absence of the tonsils and the age at which they were removed

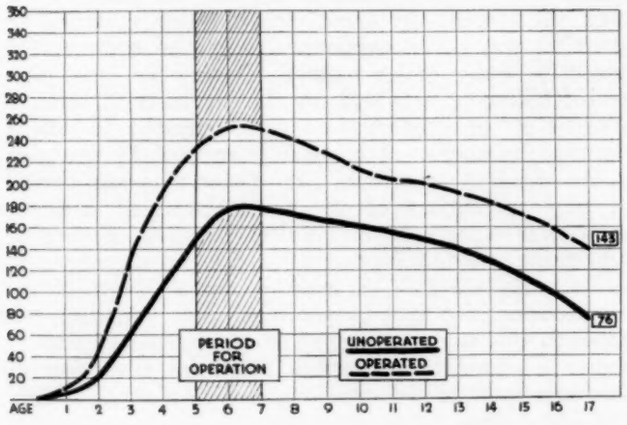

Chart 5.—Pulmonary infections (bronchitis and pneumonia) among 2,200 tonsillectomized and 2,200 nontonsillectomized children.

showed that no significant relationship could be demonstrated between the development of tuberculosis and the presence or the absence of the tonsils. When tuberculous cervical adenitis is considered it is quite clear that the tonsils are frequently a source of entrance for the tubercle bacillus and the removal of the tonsils may reduce the incidence of this tuberculous manifestation.

Children with nasal allergy, allergic involvement of the sinuses, allergic bronchitis and allergic pneumonia are not favorably influenced by tonsillectomy. Bullen [9] in a study of 2,000 children concluded that tonsillectomy does not aid in improving the results of treatment of nasal or of pulmonary manifestations of allergy. Recently Hansel and Chang [10] reached similar conclusions. They caution against the removal of tonsils and adenoids in allergic children during attacks of hay fever and against recourse to tonsillectomy with the idea of alleviating allergic symptoms.

Rheumatic manifestations in children have long been associated with infection in the tonsils. This relationship received the support of Osler in 1902, who stated "Special stress has been laid upon the tonsils as the point of entrance of the infections, as it has long been known that tonsillitis was a very frequent initial symptom. Indeed some have gone so far as to say that there is always a primary infective trouble in the lacunae of the tonsils, to which the rheumatic fever is secondary, arising from the absorption of microbes or their products." Subsequent writers stressed this relationship, which gave rise to the common dictum "the tonsil, the portal of entry of rheumatic infection." This resulted in a form of speech that became almost a platitude in the course of medical literature to the degree that it was accepted and dispensed with the regularity of an acquired habit and no doubt frequently without stopping to inquire how far it agrees with personal experiences and recurring clinical material. The various attempts to evaluate the relation of the tonsils to infections included rheumatic manifestations. These studies emanating from various parts of this country and from England agree that there is no justification in the statements that were accepted for more than twenty-five years. No unanimity exists in these studies, owing in part to a different approach, but in general it has been shown that any rheumatic manifestation may develop in a child whose tonsils have been removed prior to the first evidence of rheumatic disease. There is also complete agreement in the statement that recurrent attacks of rheumatic disease are as likely to occur in children whose tonsils have been removed as in those in whom they are still intact. There is, however, some difference of opinion as to the influence of the tonsils on the cardiac complication and on the mortality in this disease.

The survey made in Rochester gives a fair idea of the incidence of rheumatic manifestations in two large groups of children. It is noted that chorea seems not to be influenced favorably by tonsillectomy; in fact, primary attacks were somewhat more frequent in tonsillectomized children. Rheumatic fever occurred somewhat less frequently in the tonsillectomized children. This difference may be explained by the lessened incidence of throat infections in the children who were operated on. The mild rheumatic symptoms termed muscular or growing pains occurred frequently in both the tonsillectomized and the control group. Though the children who were operated on had somewhat less evidence of trouble, the difference in the two groups was not statistically significant. Rheumatic carditis was studied in the 4,400 children in a similar manner to that in which the other rheumatic manifestations were studied. The incidence of carditis did not differ much in the two groups. During the ten year period in which these children were observed, it developed that 1.1 per cent of the children contracted rheumatic carditis following tonsillectomy, while among the children whose tonsils were not removed 1.3 per cent contracted the same lesion. The difference is not significant. It would appear from the figures that tonsillectomy did not have much to offer either in the prevention or in the control of rheumatic infection. A further possible relationship of the tonsils to rheumatic infection was sought in studying the outcome of a group of rheumatic children. This observation was made on a group of 597 children who had developed their first attack of rheumatic infec-

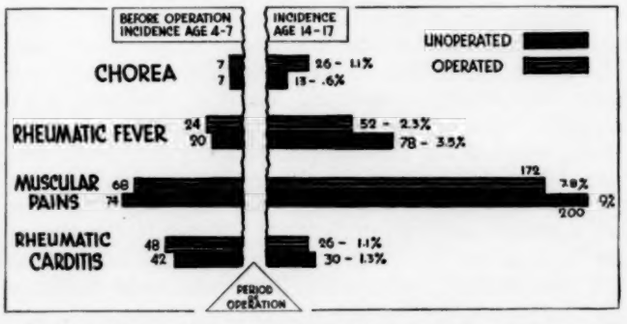

Chart 6.—Rheumatic manifestations before and for ten years after removal of tonsils of 2,200 children and for a similar period among 2,200 nontonsillectomized children.

tion between the ages of 5 and 10 years. All these children either were observed for a period of ten years after their primary attack or succumbed to the disease during this period.

In table 1 it is noted that these children could be divided into three groups: those whose tonsils were in at the time of the primary attack and remained in during the five year period of observation, those whose

9. Bullen, S. S.: J. Allergy **11**: 310 (July) 1931.
10. Hansel, F. K., and Chang, C. S.: Relation of Allergy and Tonsillectomy in Children, Arch. Otolaryng. **31**: 45 (Jan.) 1940.

tonsils were out at the time of the initial attack and those whose tonsils were in at the time of the initial attack but were removed subsequently during the five year period of observation. The mortality rate (table 2) is distinctly higher in the group of children whose tonsils were not removed. Though the recurrences were about the same in the three groups, the children who were operated on appeared to be somewhat safeguarded. A similar experience has been commented on by several clinicians, and recently Allan and Baylor [12] presented evidence to substantiate that position.

In reviewing the several studies made on the relationship of the tonsils to rheumatic disease in children it becomes evident that the surgical treatment of the tonsils, regardless of the age of the child, offers no certainty in preventing this infection and apparently does not reduce the number of recurrences. The clinical improvement in many cases has justified the operation, and the somewhat meager statistical data at hand in the Rochester study suggests that fatal carditis was noted less frequently in the tonsillectomized group.

The incidence and the complications occurring in the common infectious diseases of childhood were studied

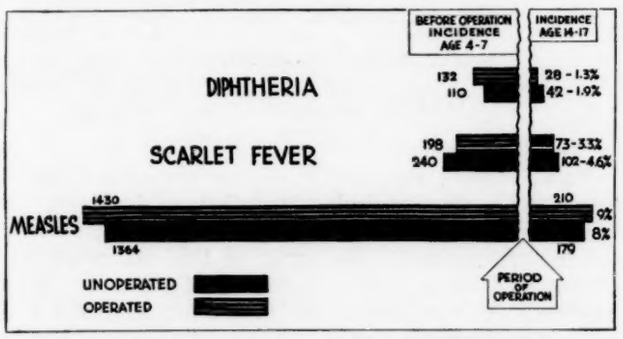

Chart 7.—Diphtheria, scarlet fever and measles before and for ten years after removal of tonsils of 2,200 children and for a similar period among 2,200 nontonsillectomized children.

in the tonsillectomized and nontonsillectomized groups. In pertussis the presence or absence of the tonsils made no difference. The same situation existed with measles. Diphtheria showed a lower incidence in the tonsillectomized children, but the incidence was low in both groups, probably owing to immunization. Scarlet fever occurred somewhat less often in the tonsillectomized children, but the difference was not significant. In a study of 267 scarlet fever patients in the hospital it was found that more complications developed in the children whose tonsils had not been removed.

The proper development of the child may be interrupted by recurrent infections or may be interfered with when normal physiologic processes such as nutrition, digestion, speech, hearing and mental development are impaired. There is abundant clinical and statistical evidence to show that either hypertrophied tonsils or infected tonsils may impair the child's nutrition. Following removal of the tonsils in these instances the nutrition of the child promptly improved. When, however, the procedure was applied to a large group of children on whom a prophylactic tonsillectomy had been performed, there was no evidence that the tonsillectomized children demonstrated a superior nutritional state. Sufficient evidence is available to show that chronically infected tonsils may definitely retard the nutritional development even if the other factors essential to good nutrition are assured a child.

Such disturbances as recurrent vomiting attacks and chronic anorexia are known to influence the development of the child unfavorably. The underlying causes of these manifestations are not always obvious. When they exist the tonsils are frequently incriminated, even before a careful search is made for other etiologic factors. Undoubtedly chronic infections in the tonsils can bring about these symptoms, for there is abundant clinical evidence that recurrent or cyclic vomiting is sometimes relieved after the tonsils of these children have been removed. Marked improvement in the appetite likewise has been known to develop when presumably infected tonsils have been removed. It does not follow, however, that tonsillectomy always assures a child freedom from the vomiting habit nor does the appetite promptly improve. A careful analysis of these complaints in a group of children before and after tonsillectomy showed that after tonsillectomy approximately 50 per cent were relieved of the attacks of periodic vomiting that had existed prior to the operation. In the case of anorexia that had been present for some time before a tonsillectomy was performed, somewhat less than 50 per cent showed improvement in appetite following the operation. In attributing the improvement to tonsillectomy one must not overlook the fact that such complaints as recurrent vomiting and anorexia disappear even when the tonsils are not removed. Certainly in some individuals diseased tonsils are the direct cause of these digestive complaints.

Impairment of hearing and irregularities in speech have been ascribed to obstructive lymphoid tissue in the nasopharynx. Hearing defects other than those produced by infection in the middle ear may be due to lymphoid obstruction of the eustachian tube. The tonsils are seldom responsible for impairment of hearing. The adenoids frequently are the cause of trouble and removing them may promptly relieve this condition. Speech irregularities have been improved in cases in which hypertrophied tonsils and adenoids have been removed, but there is no evidence that the tonsils are a disturbing factor in any large number of children with speech defects.

TABLE 1.—*Incidence of Recurrent Attacks of Acute Rheumatism with Reference to Removal of Tonsils in 439 Children Observed for Five Years*

Age of Children at First Attack	Number in Whom First Attack Developed Before Tonsillectomy	Number Who Had Recurrent Attacks	Number in Whom First Attack Developed After Tonsillectomy	Number Who Had Recurrent Attacks
Under 5 years.....	36	11-31%	2	1-50%
From 5 to 10 years...	104	42-41%	22	10-45%
From 10 to 15 years..	151	30-33%	88	19-21%
From 16 to 17 years..	25	8-32%	11	4-36%

TABLE 2.—*Effect of the Tonsils on Outcome of Rheumatic Infection in 597 Children Followed for Ten Years*

Tonsils	Number	Died	Recurred	No Recurrence
Remained in.....	156	13%	46%	41%
Out at 1st attack.....	187	7%	48%	45%
Out after 1st attack....	254	4%	44%	52%

12. Allan, W. B., and Baylor, J. H.: Bull. Johns Hopkins Hosp. **63**: 111-123 (Aug.) 1938.

There is undeniable evidence that the child population of our country has experienced better physical development with fewer interruptions due to mild and prolonged illnesses in the last three decades. Not only has the infant mortality been materially reduced but fatal illness in children of school age is less likely to occur. It is true that this saving of child life and improvement in the general health of the child has come during the period of widespread surgical treatment of the tonsils. It has even been suggested that removing the tonsils in from 30 to 50 per cent of the urban children of our country has played a major part in attaining this favorable situation. One cannot, however, lose sight of the fact that notable advances have been made in the science of nutrition during this period. The application of these discoveries has contributed appreciably to improving the nutritional state of the growing child. Likewise in the fields of bacteriology and immunology advances have been made which have greatly reduced the hazards of certain diseases, notably diphtheria, syphilis and pertussis. Perhaps of even greater importance to the child has been the widespread application of public health procedures such as pasteurization of milk, the safeguarding of water supplies and the refrigeration of foods. Health education in the schools, by volunteer and official health agencies and the utilization of the press and the radio, has reached many children and parents who formerly were kept in ignorance of the factors that safeguarded health. Due consideration must be given to all these contributing factors in assigning the reasons for the improved health of the children of America. Because of these various improvements in child care that have been made available during the last three decades, it becomes more difficult to assign to the tonsils the particular part that they play in the economy of the child.

CONCLUSIONS

The tonsils have assumed an important role in the economy of the child during the last thirty years. The beneficial results following tonsillectomy in selected cases inspired this procedure on a large percentage of children often without a good reason.

Follow-up studies on tonsillectomized and nontonsillectomized children were undertaken to show the trend of certain complaints over a ten year period in the two groups and to note the effect of the tonsils on the physical development of the child.

It was shown that markedly hypertrophied tonsils and tonsils that are repeatedly inflamed giving rise to attacks of tonsillitis and cervical adenitis frequently do impair normal physical development. When such a condition exists after the age of 4 years it is advisable to have the tonsils removed, with the expectation that at least 50 per cent of the children so treated will be materially improved.

Such infections as the common cold, otitis media, sinusitis and laryngitis may unfavorably influence the child's normal development. It cannot be demonstrated that the tonsils are often a causative factor in these infections; consequently tonsillectomy does not offer a solution for their eradication save in exceptional cases.

It could not be shown that the incidence of such diseases as bronchitis, pneumonia and tuberculosis was reduced in tonsillectomized children. The tonsils are not often responsible for pulmonary infections.

Rheumatic disease and nephritis constitute serious handicaps to a child's normal development. Recent studies show that the tonsils play a less significant role in the causation and treatment of these diseases than was formerly supposed. However, a reduction in the number of throat infections following tonsillectomy has a beneficial effect in the rheumatic subject.

There has been a significant decline in the mortality and morbidity rate of children during the last three decades. There has also been an improvement in the physical development of children in America. The application of the new discoveries in the field of nutrition, immunology and sanitation has contributed much to this favorable situation. When proper consideration is given to these factors it is evident that the tonsils are not as great a menace to a child as has been frequently suggested.

There is substantial evidence that in about 20 per cent of the children the tonsils are either hypertrophied or diseased and therefore have an unfavorable influence on the physical development of the child. Such tonsils should be removed.

16 North Goodman Street.

RESULTS OF CONSERVATIVE APPLICATION OF X-RAY TREATMENT IN CHRONIC LEUKEMIA

A NOTE OF OPTIMISM

WILLIAM P. MURPHY, M.D.

BOSTON

Forkner [1] has written "It is now almost a hundred years since the classical description of leukemia yet today we know almost nothing about its cause or its specific treatment." The truth of this statement will be evident from even a brief review of the more recent literature on the subject or of almost any series of records of patients treated according to the customarily applied technics.

The rather general tendency toward pessimism on the part of the medical profession in respect to the possible benefits to be derived from treatment of a patient with leukemia has developed, and is perhaps in part justifiable, because of the ineffectiveness of therapy in the acute and atypical leukemias which is assumed to apply to all leukemias and because of the failure of statistical studies of case records to have demonstrated that the life span of the patient with chronic leukemia has been appreciably lengthened as the result of treatment. Although the measure of the value of therapy of an illness on the basis of its effect on duration of life has a dramatic appeal it may blind us to the importance of treatment, particularly of the patient with a chronic illness, in respect to his economic and social status, general health and comfort.

In 1924 Minot, Buckman and Isaacs [2] reported data which showed little difference between the average duration of life of seventy-eight patients with chronic myelogenous leukemia treated by x-ray irradiation and fifty not irradiated. The former group lived an average of 3.5 years after the first symptoms, the latter slightly

From the Medical Clinic of the Peter Bent Brigham Hospital.

Dr. Merrill C. Sosman directly supervised the x-ray therapy, and Miss Isabel Howard made numerous blood counts.

Read before the Section on Pharmacology and Therapeutics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Forkner, C. E.: Leukemia and Allied Disorders, New York, Macmillan Company, 1938.

2. Minot, G. R.; Buckman, T. E., and Isaacs, Raphael: Chronic Myelogenous Leukemia: Age Incidence, Duration and Benefit Derived from Irradiation, J. A. M. A. **82**: 1489 (May 10) 1924.

more than 3.0 years. In the same year Minot and Isaacs [3] published similar data concerning chronic lymphogenous leukemia but found no essential difference in the average duration of life in irradiated and nonirradiated patients. A group of eighty patients composed of fifty irradiated and thirty nonirradiated lived an average of 3.45 years after the first symptoms. It was concluded that both groups were benefited symptomatically by irradiation, the myelogenous group benefiting by an average of 1.6 years of efficient life whereas in the lymphogenous group the efficiency of the patient was increased strikingly in only 10 per cent. The latter authors quote Klewitz and Schuster [4] and Brandt [5] as reporting the average duration of life in chronic lymphogenous leukemia to be about two years.

Hoffman and Craver [6] reported the average duration of life after the onset of the disease to be 3.36 years and after the beginning of treatment 2.62 years for eighty-two patients with chronic myelogenous leukemia. These authors were, however, somewhat more optimistic in regard to the other benefits to be derived from x-ray treatment and concluded that "The actual duration of efficient life after beginning irradiation averaged 2.13 years, varying from eight months to 5.66 years. The radiation treatment causes an average increase of about ten months in the duration of efficient life—a period of efficiency and usefulness that the patient otherwise could not hope to enjoy."

Arendt and Gloor [7] reported even more favorable results from therapy of both forms of chronic leukemia. The average duration of life in thirty-nine cases of chronic myelogenous leukemia was four years, and of even greater importance perhaps is the occurrence in their group of a greater number of patients living more than four years.

Although Allen and Dickey [8] have not discussed duration of life, they have been greatly impressed with the possibility of improving the patient's general condition. Their attitude is well expressed in the following sentence: "Any procedure which will increase the length of a remission, raise the degree of the patient's efficiency during a remission or prolong useful life in myelogenous leukemia deserves consideration."

This small group of references to literature dealing with the effect of therapy on the prognosis in respect to prolongation of life and symptomatic improvement tells essentially the entire story of the results of the treatment of chronic leukemia to the present time. Treatment in myelogenous leukemia has been primarily that of periodic exposure of the spleen and (or) the long bones to rather massive doses of x-rays, except in the groups reported by Forkner and Scott [9] and Arendt and Gloor,[7] in which the use of arsenic was emphasized. Little originality has been shown in respect to the method of application of treatment and little effort has been made to keep the disease process under control. Arendt and Gloor [7] have given arsenic in some form more or less continuously between relapses, which were then controlled by x-ray therapy as the need arose. Allen and Dickey [8] have emphasized the importance of following the patient's condition carefully by means of frequent analysis of the condition of the blood and by saliva leukocyte counts, but they state that, "As a general rule, a series of treatments should be initiated only when the patient's general condition is poor and his efficiency low." This method of determining the use of treatment has been subscribed to by Minot, Buckman and Isaacs,[2] Hoffman and Craver,[6] Forkner [1] with reservations and Jackson,[10] who states that treatment of chronic myelogenous leukemia should be withheld until such time as the patient's symptoms appear to call for alleviation. In discussing the treatment of chronic lymphogenous leukemia, Jackson [10] makes the comment: "As with chronic myelogenous leukemia, irradiation of the spleen or chest, preceded by blood transfusions if there is a coexisting anemia of moment, is the treatment of choice. It is very questionable, however, whether there is any advantage in treating those patients who are symptomless. The details of the x-ray therapy should be left to the radiologist in charge . . ."

This attitude toward the use of x-ray therapy is that which has largely influenced the regulation of treatment up to the present time and which is probably largely responsible for the belief held by many clinicians that the patient with chronic leukemia is not in better condition with a low than with a high leukocyte count. It is quite obvious that with the method of therapy often employed such might be the case. Massive x-ray dosage is applied over the spleen at a time when the patient is weakened, often suffering from anorexia and nausea and with a high leukocyte count. The therapy may increase the anorexia and nausea, the leukocyte count may drop rapidly even to a subnormal level and the hemoglobin and erythrocyte levels may drop, which increases the feeling of weakness and malaise so that it may take days, weeks or even months to recover from the effects of treatment, at the end of which time and just when the patient has begun to feel fairly well his leukocyte count is again rising, symptoms returning and he is put through another third degree of treatment. And thus many of our patients go through a series of relapses and remissions feeling more disturbed than relieved by therapy, dreading each successive series of treatments more and more, frequently to the point of avoiding the physician's check-up until it is too late to hope for much benefit. The periods during which the patient experiences a feeling of well being of sufficient degree to allow the pursuit of normal activity are short and generally progressively shorter, and the periods of sickness during and following x-ray therapy either in or out of a hospital are discouraging and expensive ones. Exceptions to this course do occur. Spontaneous remissions of longer or shorter duration may be experienced by the patient with either form of leukemia with and without therapy, but these are not the rule and do not affect the course of the illness of the majority of patients.

With these facts in mind and after having observed the unfavorable general condition of a group of patients with chronic leukemia treated in the generally accepted manner, it seemed desirable to consider wherein this form of treatment was at fault and then to correct these faults as far as possible.

3. Minot, G. R., and Isaacs, Raphael: Lymphatic Leukemia: Age Incidence, Duration and Benefit Derived from Irradiation, Boston M. & S. J. **191:** 1 (July 3) 1924.

4. Klewitz, F., and Schuster, E.: Zur Prognose der Leukämie, Deutsche med. Wchnschr. **48:** 1003 (July 28) 1922.

5. Brandt, T.: Roentgen Ray Treatment of Chronic Leukemia, Norsk. mag. f. lægevidensk. **84:** 761 (Sept.) 1923; abstr. J. A. M. A. **81:** 1916 (Dec. 1) 1923.

6. Hoffman, W. J., and Craver, L. F.: Chronic Myelogenous Leukemia: Value of Irradiation and Its Effect on Duration of Life, J. A. M. A. **97:** 836 (Sept. 19) 1931.

7. Arendt, J., and Gloor, W.: Resultate der Röntgenbestrahlung bei chronischen Leukämien, Strahlentherapie **44:** 715, 1932.

8. Allen, K. D. A., and Dickey, L. D.: The Saliva Cell Count in Myelogenous Leukemia, Am. J. Roentgenol. **38:** 57 (July) 1937.

9. Forkner, C. E., and Scott, T. F. M.: Arsenic as a Therapeutic Agent in Chronic Myelogenous Leukemia, J. A. M. A. **97:** 3 (July 4) 1931.

10. Jackson, Henry, Jr.: The Leukemias, New England J. Med. **222:** 22 (Jan. 4) 1940.

The most obvious and serious fault appeared to be that of allowing the patient to develop repeated relapses during which the disease process has progressed, followed by intensive treatment at a time when the general condition is poor. The well treated patient with diabetes or pernicious anemia is not permitted to omit treatment until severe acidosis or relapse occurs but is maintained constantly in as nearly a normal condition as is possible. Why is it not equally logical to prevent relapses and to maintain as nearly as possible a normal condition for the patient with chronic leukemia? In order to accomplish this the patient is advised to report each month for a blood examination. If the leukocyte count shows a tendency to rise during successive counts or if it has reached a level of about thirty to forty thousand, one x-ray treatment is given. consultation with the roentgenologist, but the patient's physician will constantly guide the course of therapy because the roentgenologist may not be equipped to do blood counts and may not be so familiar with the patient's general condition.

The size of the x-ray dose and the site to be treated offered another problem for consideration. Severe anorexia, nausea and vomiting frequently follow massive therapy applied over the spleen, to a mass of lymph nodes or over the chest, and yet a similar dose over the long bones was often less disturbing to the patient but the effect on the leukocyte count, mass of lymph nodes or spleen was essentially the same. It would appear to be logical therefore to avoid the disturbing upset of the patient by the use of smaller dosage, provided an equally good effect can be produced. By apply-

TABLE 1.—*Data Concerning Seven Patients with Chronic Lymphogenous Leukemia Treated by Means of Small Doses of X-Rays Applied by the Spray Technic* *

			Duration Since First						
			Symptoms		Diagnosis		Basal Metabolic		
Patient	Age	Sex	Years	Months	Years	Months	Rate	Complications	Cause of Death
1. A. B.	55	♀	12	—	9	—	— 1	Recurrent herpes	Pneumonia
2. P. K.	63	♀	11	9	7	6	+ 2	Hypertension; arthritis	
3. J. C.	49	♂	10	6	9	6	— 3 +13	Arthritis	
4. M. D.	55	♀	5	—	4	—	—	Cardiac hypertension	
5. A. E. B.	57	♀	2	6	1	6	+34	Pneumonia	
6. A. S.	70	♂	2	—	1	9	—	Deafness	Hemorrhage
7. L. H.	63	♂	1	9	1	7	—	Orchitis	

* An effort has been made to hold the leukocytes at low levels throughout the course of the illness.

TABLE 2.—*Data Concerning Nine Patients with Chronic Myelogenous Leukemia Treated as Were the Patients of Table 1*

			Duration Since First						
			Symptoms		Diagnosis		Basal Metabolic		
Patient	Age	Sex	Years	Months	Years	Months	Rate	Complications	Cause of Death
8. N. J.	51	♂	5	—	5	—	—	.....	Pneumonia
9. M. R.	36	♀	4	9	4	3	+16	.....	Hemorrhage
10. A. L.	49	♀	4	6	3	6	+52	Diabetes mellitus; hypertension	
11. J. T.	33	♀	4	6	—	5	—	.....	Cerebral embolus
12. A. R.	42	♀	4	—	2	—	+34	Pulmonary tuberculosis	Pulmonary tuberculosis
13. W. B.	47	♂	3	6	3	6	—	Terminal diabetes mellitus	Cerebral thrombosis
14. J. S.	59	♀	3	6	3	6	+17		
15. M. McG.	65	♀	3	4	2	8	+68	Myocarditis	Not known
16. M. D.	65	♀	3	3	3	3	+33	Hypertension; pneumonia; herpes zoster	Pneumonia

If the rise has been gradual the patient returns for a leukocyte count at the end of a week; if rapid or if the count has risen above about forty thousand a count is done on the day following treatment. If in either case the leukocyte level has not dropped sufficiently, another treatment is given. In each instance an effort is made by this means to maintain the leukocyte level as near normal as possible constantly and never to allow it to rise above forty thousand. X-rays applied in this way rarely produce distressing nausea and the patient's condition remains rather uniformly good except as it may be influenced by intercurrent infections or other complications. Care must be taken to avoid too great a drop in the leukocyte count as the result of overdosage with x-rays. This will rarely occur if each treatment is preceded by a leukocyte count, and if there is then any question with regard to the advisability of further exposure an interval of a few days or a week may be allowed, at the end of which another count is done. The exact treatment which is to be given will be decided in ing this small dose over a large part of the body surface it was found possible to do this and thereby to avoid on most occasions the disturbing post-treatment effects. Mild anorexia and nausea have followed treatment of the very sensitive patient and on rare occasions of any patient, but a severe unpleasant or incapacitating reaction has rarely occurred. The use of small dosage and the application of the x-rays over the greater part of the body from a distance, so-called teleoroentgen therapy, have both been advocated previously and both are now being used for the treatment of leukemia in several clinics, but their value as opposed to the massive dose method has not been widely enough recognized and the method has not come into general use.

The principles here set forth for the treatment of the patient with chronic leukemia have been applied as far as possible to a small group of patients and the results as far as age, sex and duration of life is concerned are shown in tables 1 and 2. For comparison with the groups shown in tables 1 and 2 there is pre-

sented in tables 3 and 4 groups essentially similar but treated largely by massive dosage, periodically as symptoms of progression of the disease state indicated without the attempt at complete control of progress as in the two former groups. There is not a sharp line of distinction between the method of treatment or follow-up in certain individual cases in the two groups and one might question the decision to include them in one table as opposed to the other. For example, patient 6 included in table 1 lived on a farm in Canada which made it difficult for him to return sufficiently often for treatment to be given to maintain the blood in a satisfactory state. On the other hand his x-ray therapy was given in small doses over the entire body except for two exposures to the cervical region at a time when the glands in this region were greatly enlarged. His death followed a severe hemorrhage from the gastrointestinal tract. This occurred during the middle of winter, 20 miles from his physician, who found it impossible to give him a transfusion of blood. Even though he was then 72 years of age, life might have been prolonged had circumstances been different.

Arsenic in the form of solution of potassium arsenite has been used from time to time in several of the group of patients with myelogenous leukemia of table 4. The effect has been to decrease the leukocyte count from the height of the peak during relapse, as was shown to be possible by Forkner and Scott,[9] but there has been no evidence that it is possible to maintain the leukocyte count at a low level for a longer period of time than is the case following x-ray exposure. The most striking effect of the arsenic has been to upset the patient to such an extent that the treatment was far more disturbing than the symptoms of the disease. Anorexia and mild nausea are almost constant during its use, severe nausea and diarrhea frequent occurrences. An example of its effect is found in a case that came to my attention after approximately three years of arsenic therapy with a high leukocyte count. Anorexia and mild nausea were present almost constantly during this time, the patient being scarcely able to eat a meal and having lost 40 pounds (18 Kg.) during the last year of treatment. Following a few x-ray exposures by the "spray" technic the leukocyte count dropped to a normal level, the patient's appetite improved immediately and he regained within a few months the 40 pounds lost. Solution of potassium arsenite may be of value for the patient who does not have access to x-ray therapy but is probably less desirable than x-rays when this form of treatment is available.

In practically all instances, the patients listed in tables 1 and 2 have had leukocyte counts done frequently and an effort has been made to control these levels and the patient's general condition by x-ray treatment at intervals as indicated. Each treatment, with rare exceptions, since early in 1934 has been applied over the entire body, alternately front and back, supplying about 50 to 60 roentgens per dose. In general the treatment may be described as follows: 200 kilovolts, 100 cm. distance, 0.5 mm. of copper filter, spray technic.

Data concerning seven patients with chronic lymphogenous leukemia treated in the approved manner are shown in table 1, and concerning ten patients by the older method in table 3, a total of seventeen. Data concerning nine patients with chronic myelogenous leukemia treated in the approved manner are shown in

TABLE 3.—*Data Concerning Ten Patients with Chronic Lymphogenous Leukemia Treated by Massive Doses of X-Rays at Intervals for Control of High Leukocyte Counts and Symptoms Produced by Progression of the Disease*

Patient	Age	Sex	Duration Since First: Symptoms Years	Symptoms Months	Diagnosis Years	Diagnosis Months	Basal Metabolic Rate	Complications	Cause of Death
17. V. A.	59	♀	9	—	9	—	—	.....	Not known
18. K. H.	68	♀	4	10	4	10	—	.....	Not known
19. C. G.	70	♀	4	6	4	3	— 3	Herpes zoster	Not known
20. A. G.	56	♀	4	—	4	—	—	Pneumonia	Not known
21. C. P.	48	♂	3	6	3	3	+33	Severe anemia	Leukemia; hemorrhage
22. G. S.	61	♂	2	9	2	3	—	Herpes zoster; hydrothorax	Leukemia
23. I. S.	65	♂	1	9	1	6	+23	.....	Not known
24. S. G.	54	♀	1	5	1	4	+48	Hydrothorax; severe anemia	Not known
25. D. C.	68	♂	1	2	—	2	+19	.....	Leukemia
26. J. C.	46	♂	1	—	1	—	—	Severe anemia	Not known

TABLE 4.—*Data Concerning Eleven Patients with Chronic Myelogenous Leukemia Treated as Were the Patients of Table 3*

Patient	Age	Sex	Duration Since First: Symptoms Years	Symptoms Months	Diagnosis Years	Diagnosis Months	Basal Metabolic Rate	Complications	Cause of Death
27. W. McG.	35	♂	4	4	2	4	—	.....	Not known
28. A. P.	37	♂	3	6	2	6	—	Cardiac	Pulmonary congestion
29. H. L.	21	♀	3	—	2	—	+33	Pregnancy	Not known
30. J. C.	32	♂	2	11	2	10	—	Extraction of 2 abscessed teeth	Not known
31. A. B.	60	♀	2	10	2	10	—	Mild diabetes	Coronary infarction
32. A. G.	51	♀	2	8	2	8	+29	Hypertension; mild diabetes	Not known
33. E. G.	73	♀	2	7	2	3	+54	Herpes zoster	Not known
34. L. S.	53	♀	2	—	1	9	+33	Extraction of 8 teeth	Not known
35. W. B.	24	♂	2	—	1	2	—	Exposure to benzene fumes	Pneumonia? embolus, pulmonary?
36. A. B.	59	♂	1	6	1	6	+36	Extraction of 2 teeth	Not known
37. G. D.	33	♂	—	9	—	4	+40	Healed pulmonary tuberculosis	Multiple infarcts and thromboses

table 2, and concerning eleven patients by the older method in table 4, a total of twenty. The number of cases reported in any of the groups is too small to allow the data to be considered statistically, and as this report is not concerned with the analysis of leukemia in general they will not be discussed in detail. It is of

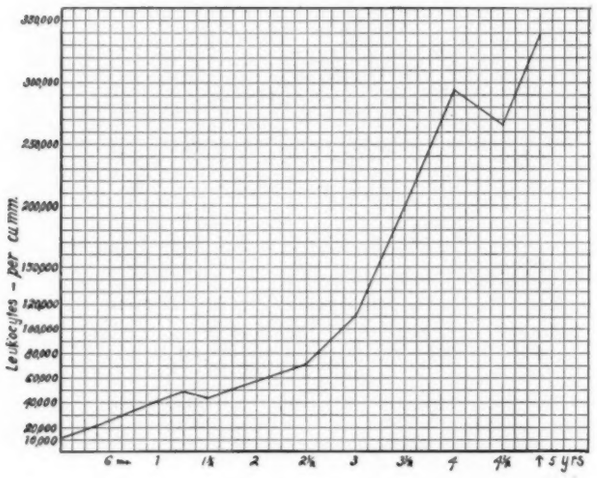

Chart 1.—Course of the leukocyte count in case 3 of table 1 during five years' observation before x-ray treatment was started.

interest to note, however, that myelogenous leukemia appeared at an earlier age in many instances than did the lymphogenous form; that of the seventeen lymphogenous eight were male, nine female and of the twenty myelogenous eight were male, twelve female; that the basal metabolic rate was increased more uniformly in those in whom the test was made in the myelogenous than was the case in the entire lymphogenous group; and that the most commonly observed evidences of the disease in its earlier stages were enlarged lymph nodes or a mass in the left abdomen; continuous or intermittent fever of unknown origin; anorexia, nausea or vague gastrointestinal disturbance; and definite, often striking loss of weight. Pulmonary tuberculosis pre-

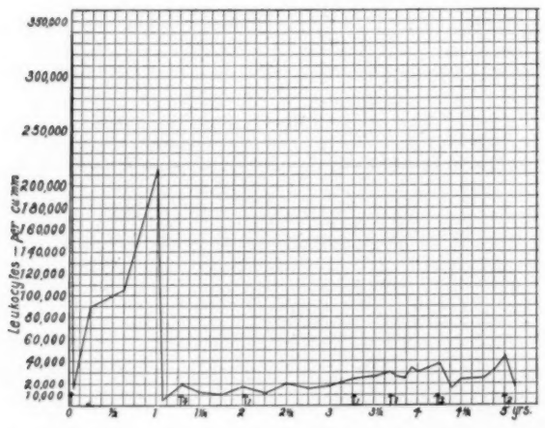

Chart 2.—Course of the leukocyte count in the same patient as of chart 1 is shown during five years of treatment with x-rays at intervals necessary to maintain the leukocyte level below about 40,000. The arrows indicate the time of x-ray treatment, the figure beside the arrow the number of exposures.

ceded the onset of leukemia in two of the myelogenous groups. A pneumothorax had been produced on the right side in patient 12 of table 2 but after four years of leukemia and shortly before death x-ray examination showed extensive involvement of the left lung. A postmortem examination was not made. Patient 37 of table 4 developed leukemia while in a tuberculosis sanatorium. At postmortem examination the tuberculosis was described as healed. Three instances of myelogenous leukemia were basophilic (table 2, cases 14 and 16; table 4, case 31). Uric acid determinations were made on the blood of four of the lymphogenous group with the results 3.3, 3.6, 5.2 and 5.7 mg.; and in five of the myelogenous group with the results of 3.4, 4.6, 6.0, 6.2 and 6.7 mg. per cubic centimeter.

It is difficult to compare the longevity of the two groups with either form of leukemia with each other or with the reports from the literature previously mentioned, but in general the showing of the group in table 1 is definitely better than that of those in table 3. The duration of life has been five years or longer in four patients of the first group, whereas only one of the second group lived five years or longer. Taking into consideration the fact that all but two of those in table 1 are living and in good condition at the present time, and allowing for the possibility that the disease may be present in mild form in some of these, the result compares favorably with that of previously reported groups. But even though one may question whether or not much has been gained in respect to length of life, the members of the group shown in table 1 have during

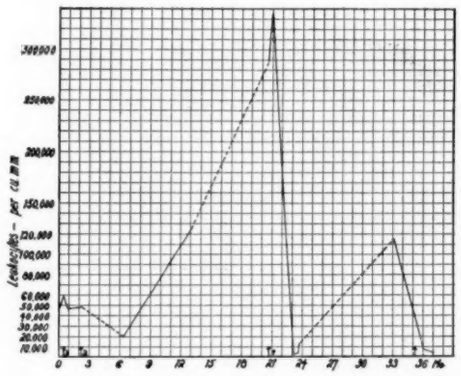

Chart 3.—Course of the leukocyte count in case 21 of table 3 during treatment at intervals by massive dosage of x-rays. The arrows and figures beside them indicate the time given and number of x-ray exposures.

life remained essentially well and able to carry on their daily duties without interruption except during the occurrence of a complicating illness. The female patients have continued with their household duties, patient 7 has continued actively with his ministerial duties and patient 3 has returned to his former occupation as a bus driver after having been relieved from duty for several years because of severe rheumatoid arthritis which antedated the leukemia. The arthritis has been completely controlled so that for three or four years hard labor has been possible without undue fatigue. The course of this patient's leukocyte levels during a period of five years before treatment was started is shown in chart 1 and for five years under treatment in chart 2. Since x-ray therapy was started the leukocyte level has been maintained below 40,000 by repeated exposures as shown in chart 2. In contrast to this patient's course is the irregular swing of the leukocyte levels of patient 21, table 3, whose clinical course was equally unstable (chart 3). The periods of remission with anything approaching normal vigor were short, a matter of a few weeks, rarely months, in the entire group shown in table 3.

The story of the two groups with myelogenous leukemia is not unlike that which has been described for the

lymphogenous groups except that the duration of life was not so long in either group (tables 2 and 4); but even so that of the patients of table 2 treated in the approved manner is longer on the average than that of the group in table 4 or of several of the series reported in previous literature. The course of the disease in the patients of table 2 has not in each instance been so smooth as that of the group with lymphogenous leukemia (table 1) and yet the majority have been remarkably well and practically throughout the duration of their life have carried on their normal duties except when handicapped by intercurrent disease. An example of the course of the leukocyte levels in a patient of this group is that of patient 13, table 2, shown in chart 4. Although this patient lived only three and a half years he continued actively at work as a model maker in a brass foundry and stopped only when a few days before his terminal illness he complained of severe abdominal and head pain. The urine suddenly became loaded with sugar and he became comatose and died a few days after admission to the hospital for the first time. At postmortem examination cerebral thrombosis was given as the cause of death. In contrast to this patient's excellent health and control throughout life there is shown in

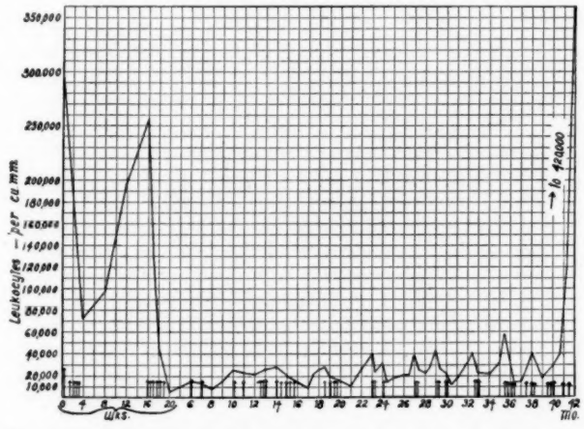

Chart 4.—Course of the leukocyte count in case 13 of table 2 as it was controlled by repeated small doses of x-rays. Each arrow indicates an x-ray exposure supplying approximately 50 roentgens applied by the spray technic.

chart 5 the pendulum-like rise and fall of the leukocyte levels of patient 28, table 4, who lived the same length of time from the onset of the disease but who was at almost no time well, was unable to resume any of his normal activities and spent much time in the hospital. As in the lymphogenous group, most of those of table 4 were more sick than well whereas most of those of table 2 lived a rather comfortable life.

The regularity of recurrence of the periods of marked increase in the leukocyte levels which commonly occurs in patients not completely controlled is well illustrated in chart 5. The interval between the peak of the rise in each relapse was approximately three months throughout the duration of the illness. The duration of this interval varies from patient to patient, but it is likely to remain rather constant in a given individual and may be influenced to some extent by the treatment used.

A six months interval between the several leukocyte peaks was observed in patient 16 of table 2 as shown in chart 6, in whom x-ray treatment was applied by the spray technic but who did not report for observation sufficiently often to allow the leukocyte level to be controlled. Three periods of rather serious illness including severe upper respiratory infection, herpes zoster and pneumonia prevented return at the proper interval on three occasions.

Patient 11 of table 2 received treatment only at the beginning of the last five months of her life, having had a spontaneous remission of four years' duration.

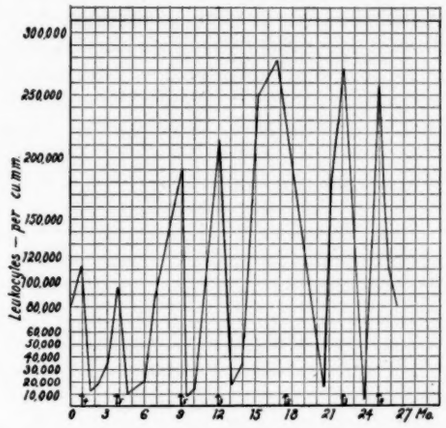

Chart 5.—Course of the leukocyte count in case 28 of table 4 as influenced by interval massive doses of x-rays. The arrows and figures beside them indicate the time given and number of x-ray exposures.

Although essentially well during the last five months she died suddenly on the fifth day following a minor operation, apparently from a cerebral embolus. A postmortem examination was not made. Her case report possibly should not be included in either group but this is done in order that the series may be entirely consecutive and inclusive.

Isaacs [11] has suggested that the effect of x-ray irradiation is to be considered as a stimulative one, in small doses causing division and in large doses causing maturation and death of the leukocytes from senility. The results observed in the treatment by the spray technic in relatively small dosage as used in the cases reported in tables 1 and 2 confirms at least to some extent this concept (chart 6). It has been observed

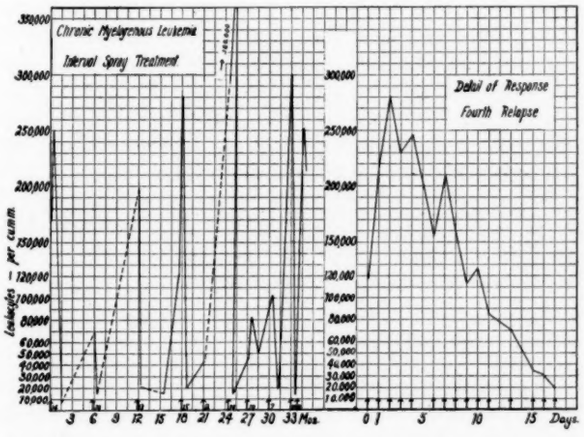

Chart 6.—Course of the leukocytic count in case 16 of table 2. X-ray treatment was given by the spray technic but control was bad because of the patient's failure to return for counts at proper intervals. In the right hand portion of the chart is shown the detail of the leukocyte response to therapy. Each arrow indicates an x-ray exposure supplying approximately 50 roentgens by the spray technic. The figures beside the arrows in the left hand portion of the chart indicate the number of exposures.

in these groups that the leukocyte level has tended to increase, often strikingly, during the few days following initial therapy after a relapse and that the per-

11. Isaacs, Raphael: Maturing Effect of Roentgen Rays on Blood-Forming Cells, Arch. Int. Med. **50**: 836 (Dec.) 1932.

centage of young or immature cells increases at first, to decrease gradually with a shift to more mature forms as the total leukocyte count drops to a near normal level. In several cases in which the leukocyte counts reached entirely normal levels the differential counts failed to show any immature, although some young forms. With repeated small dosage given as the levels tended to rise, the differential count has in many instances remained remarkably near normal for long periods of time. The nature of the response of the leukocytes to small x-ray dosages and the fact that it is possible to maintain them rather constantly at low levels with repeated exposures to small quantities suggests that chronic leukemia results from a deficiency of some substance necessary for maturation and (or) origination of leukocytes much in the same manner as pernicious anemia results from a deficiency of an antipernicious anemia factor. The deficient factor in leukemia is supplied in some manner by the x-ray exposure in small dosage, probably less satisfactorily by large dosage, which may also act to destroy cells. No doubt there is some more satisfactory means of supplying the "antileukemia" factor than by x-rays which may in themselves injure tissue. Future work should supply this substance, which will probably not be in the nature of benzene or its derivatives, the use of which is to be discouraged because of their known toxic effects, perhaps at times actually precipitating the disease state.

Another point of some interest in these patients is that in case 35, table 4, the leukemia developed after a period of definite exposure to benzene fumes. Cases similar to this have been reported by several authors previously. Two patients had been exposed to and felt keenly aware of the presence of illuminating gas fumes. Patient 13, table 2, worked for several years closely exposed to gas fumes and patient 14, table 2, had noticed leakage of gas from a kitchen range and had become acutely ill from this on several occasions. Several members of both groups had been exposed to some leakage of gas but the majority of patients who have come under my observation showing a leukemia-like blood picture, which might be interpreted as resulting from exposure to either illuminating gas or benzene fumes, have had a more acute course. It is possible that persons highly susceptible to benzene fumes may get sufficient exposure from traces of benzene in illuminating gas to develop the several evidences of disturbance in the blood which may follow exposure to higher concentrations. Further study of the concentration of benzene in canned foods and developed in limited areas from adhesive substances and in the illuminating gas from leaky fixtures may add to our knowledge of the etiology of leukemia and other blood dyscrasias of an atypical form.

SUMMARY

It is proposed that treatment of the patient with chronic leukemia be so applied and regulated that the disease state is kept constantly under control with avoidance of the severe relapses which so frequently occur. The method suggested is the frequent determination of the leukocyte level followed by x-ray exposure sufficiently often to maintain the level as near normal as possible. X-ray therapy is applied in small dosage by the "spray" technic in an effort to avoid severe reactions.

Data particularly recording the duration of life in two small groups of patients with chronic lymphogenous and myelogenous leukemia respectively who have been treated in large part by the method described were compared with data concerning two similar groups treated by the more generally used interval, massive dose method.

Not only is there suggested some advantage in respect to longevity in the former groups as opposed to that of the latter, but the general health and economic efficiency of the patients of the former has been strikingly better throughout the duration of the illness than has been the case in the groups treated by the older methods.

311 Beacon Street.

ABSTRACT OF DISCUSSION

DR. IRVING S. WRIGHT, New York: The chairman would like to ask whether any thought has been given to estimating how long the average patient has the disease before it is discovered. An answer to this question would have to depend on careful histories of individuals who had had repeated blood counts and physical examinations for other causes but which were negative for leukemia so there could be some estimation as to how long the disease was present, or at least when the patient was last known to be normal. I think that might influence to some degree statistics as to years that the patient lived, although it would be a factor that would be constant in both of Dr. Murphy's series.

DR. PAUL REZNIKOFF, New York: I do not see how one can tell how long a patient actually has had leukemia when we know how often leukemia is diagnosed in a routine examination. In fact, very often the patient shows a large spleen that he never suspected. One can determine how long a patient has had symptoms from the time he began his symptoms to the time one saw him and made a diagnosis of leukemia. I feel that most of the patients with acute leukemia have had leukemia for a longer period than they actually admit being sick. Since we do not know the etiology we are forced to treat patients either according to symptoms or hematologic observations or, better, both. I have used a good deal of spray radiation for my patients and I agree with Dr. Murphy that in general it has given more satisfaction than the massive localized therapy. But I feel that, patients differing so, it is important to determine therapy not on the basis of any routine but on what the patient shows at the particular time and how the patient responds to the particular therapy at a given time. I have had some patients whom spray radiation has never helped and even made them sick, although the majority of patients have been able to stand spray radiation much better than they could spot or localized radiation. I have given about 50 roentgens as a rule. X-rays are toxic. One cannot give x-ray therapy over a long period of time without careful check of the patient and his blood count. I believe it is necessary to check not only the white blood cell count but also the platelets and the red cells and hemoglobin. I should like to ask Dr. Murphy whether in his so-called continuous therapy he has had patients who have developed anemia or thrombocytopenia with purpura which he might attribute to the method he used.

DR. CLAUDE E. FORKNER, New York: Leukemia is a disease of unknown cause and without satisfactory treatment. For ten years some workers have been trying to irradiate large areas of the body with so-called spray or teleroentgen therapy. This followed the observation of Levin in 1922 and Minot and Spurling in 1924 that the effect of irradiation on the blood is dependent to a large extent on the square surface of entry of the rays into the organism. It should not be forgotten that not only the favorable but also the unfavorable effects are dependent on these same factors. Spray irradiation is at times useful but it is also dangerous, and especially in leukemia it must be applied with caution. Single doses of 50 or 60 roentgens in some patients will bring about severe leukopenia and thrombocytopenia and will accentuate the anemia. There is marked variation in individuals in their response to a given dose of irradiation. The leukocyte count alone is not a safe guide to follow. The

thorough study of each patient as a whole over a reasonable length of time, taking into consideration all the available information in the history, physical examination and laboratory studies, provides a far better index for selection of cases for appropriate treatment than to use any one factor as a guide. In our present state of ignorance we are not justified in regarding leukemia as comparable to diabetes or pernicious anemia as mentioned in Dr. Murphy's paper, with regard either to its etiology or its treatment. Dr. Murphy has stressed an important point which has been too little appreciated, namely that patients should not be permitted to suffer relapses of their disease if that can be prevented. By carefully following the patient as a whole, his body weight, his general feeling of well being, the size of his spleen, his liver, his lymph nodes, his evidence of increased basal metabolism, leukocyte count, thrombocytes, erythrocytes and the degree and immaturity of his white cells, one can frequently forestall the relapse by appropriate treatment. This has long been the method of choice. I cannot agree with Dr. Murphy that the most striking effects of treatment with arsenic are to upset the patient. Solution of potassium arsenite (Fowler's solution), when given properly, almost without exception is a valuable therapeutic agent in chronic myelogenous leukemia. Solution of potassium arsenite must be given well diluted in fruit juice and must be given immediately after meals. The initial dose should be about 4 or 5 minims (0.25-0.3 cc.) three times daily, gradually increasing to an effective dose.

DR. H. J. ULLMANN, Santa Barbara, Calif.: As a radiation therapist it is gratifying to hear for the first time an internist say that one should control the radiation treatment of leukemia by the blood count and to treat with small doses rather than by massive doses the patient's symptoms. In lymphatic leukemia I depend more on the differential rather than on the total count because of the necessity for maintaining a sufficient number of polymorphonuclears to combat infection. In myelogenous leukemia the total count is of more importance with regard to reinstituting treatment, and frequently when the count is up, but there are no symptoms, such as an enlarged spleen or symptoms of discomfort, the judicious use of solution of potassium arsenite will carry the patient for months before further irradiation is needed. Many radiation therapists consider it wrong to give large or massive doses, and I feel that no dose should be given that makes the patient the least bit sick. I do not know whether general body irradiation is better than local, but I do know that in no instance should large doses be given. The basic dose that I use is from 50 to 100 roentgens measured on the skin, which is approximately 70 per cent of what is usually referred to in the literature as measured in air. The repetition of the dose, daily or otherwise, depends entirely on the blood count, which is made daily at first when the treatments are given daily, and, of course, the blood count must be made at the same time of day. No treatment is repeated until the count is known. I often find it difficult to get cooperation from an internist after the first course of irradiation because he turns to his textbook and if the count is not up to ten or fifteen thousand he does not refer the patient for either irradiation or consultation. The regulation of the dose and its timing should be in the hands of a radiation therapist, for if he is not a clinician he is not fit to treat with radiant energy. I do not think that, properly used, radiant energy is toxic in these cases. It can be used indefinitely if the doses are small enough. I have never seen thrombocytopenia caused by proper radiation therapy. If it did occur from such a cause I should consider that there had been gross overdosage. I did not know that any one believed one could produce an effect on the blood alone by irradiation. I have irradiated the blood in a rabbit's blood vessel, thoroughly isolated from the body, with enormous doses without producing any change in the cell count.

DR. WILLIAM P. MURPHY, Boston: Dr. Reznikoff asked with regard to my experience in respect to the development of anemia and thrombocytopenic purpura in the patients treated by means of small doses of x-rays applied by the "spray technic." There has been no greater tendency to the development of anemia in this group than in those patients receiving roentgen therapy in larger dosage over a more limited area. The erythrocyte and hemoglobin levels have in most instances been higher following treatment than they were preceding it; but this cannot be interpreted too broadly because the development of anemia in the patient with leukemia varies greatly and is governed by factors not entirely dependent on x-ray exposure. Purpura has not developed following therapy in any of this group of patients. Severe and alarming leukopenia has developed in two or three patients treated in the hospital but not under my immediate observation. This condition is evidence of an overdosage of x-rays. If not extreme the leukocytes will gradually increase in numbers without specific therapy. If the leukopenia is severe, transfusions will usually keep the patient out of danger until regeneration occurs. One point which has been reemphasized and which applies in principle to the control of most chronic illnesses is that the best results will be obtained only with a careful and critical evaluation of the patient's entire blood and clinical picture throughout the period of illness.

HUMAN SERUM TRANSFUSIONS

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AND
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Moon [1] states that shock is "a circulatory deficiency, not cardiac or vasomotor in origin."

One of the fundamental requirements in combating shock is restoration and maintenance of adequate volume of the circulating blood. Whether shock is primary or secondary, whether due to hemorrhage, trauma or toxic substances, it is generally believed that there is a resultant diminished circulating blood volume and decreased peripheral blood flow. In the presence of dilated and more permeable capillaries, there is progressive blood stasis and subsequent loss of plasma into the tissue spaces. Thus the oxygen supply to the tissues is greatly curtailed. This course of events is progressive unless interrupted. One means of interrupting this sequence is to administer sufficient fluid to restore adequate circulating volume and improve the rate of blood flow. Furthermore, it is imperative that the vicious circle of progressively diminishing blood volume and blood flow and tissue anoxia should be interrupted as early as possible before severe and irreversible damage to the tissues occurs.

In the past, the most common fluids employed to combat shock have been crystalloid solutions such as dextrose, saline-dextrose and Ringer's solution. As was demonstrated in a series of experiments reported previously,[2] the crystalloid solutions are of only temporary beneficial effect. They increase blood volume but, owing to the fact that they do not remain in the circulation, their beneficial effects are only transient. When such crystalloid solutions diffuse out of the abnormally permeable capillaries the increasing edema is decidedly harmful. Acacia solution has been employed because this material remains in the circulation owing to its colloidal properties, but immediate and delayed reactions [3] contraindicate its use.

Read before the Section on Pathology and Physiology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

From the Samuel Deutsch Serum Center, Departments of Obstetrics and Gynecology, and the Department of Gastro-Intestinal Research, Michael Reese Hospital.

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Blood transfusion has been the most acceptable measure in shock therapy. In profound shock, however, urgency in the administration of fluid is vital. The delay involved in securing blood and in the necessary laboratory tests of typing, compatibility and the like diminishes the value of blood transfusions, for in this time interval the state of shock may become irreversible and fatal. Even when bank blood is available there is an unavoidable delay in performing laboratory tests.

In a previous publication [2] we demonstrated that serum is an effective agent in combating shock resulting from hemorrhage. Observations on experimental animals revealed that serum transfusion was almost as effective as blood transfusion in overcoming shock and in preventing acidosis and death in animals subjected to severe repeated hemorrhage. Under the same experimental conditions, physiologic crystalloid solutions were ineffective.

Experience by one of us (S. O. L.) with the preparation and use of human serum in the past ten years in the treatment of various infectious diseases has demonstrated the safety and innocuousness of administering large amounts of pooled human serum without preliminary typing and compatibility tests. Following the experimental work referred to previously, we did not hesitate to give transfusions of pooled human serum to patients for various conditions. This paper is a report on forty-seven patients to whom serum was given for a variety of medical and surgical conditions. In many cases the serum transfusions were an emergency measure which did not allow for detailed laboratory determinations. However, clinical observations were made and recorded. Further work in this field of serum transfusions will include laboratory studies on the blood.

EMERGENCY TREATMENT OF HEMORRHAGE AND SHOCK

Sixteen patients received serum transfusions in the emergency treatment of hemorrhage and shock (table 1). Eight of these cases were obstetric, seven surgical and one medical. Various amounts of serum were given, varying between 450 and 1,400 cc. In several instances the response to serum transfusion was dramatic, and we feel that it was a life saving measure. In these instances the patient's condition was extremely grave, and the immediate administration of serum effectively overcame the shock. In all instances a beneficial effect from the serum transfusion was observed. A brief report on three demonstrative cases follows:

TABLE 1.—*Human Serum Transfusions in the Emergency Treatment of Hemorrhage and Shock*

Case	Age	Cause of Hemorrhage	Degree of Shock	Estimated Blood Loss	Blood Pressure in Shock	Amount of Serum Given, Cc.	Blood Pressure After Serum Transfusion	Clinical Response to Serum Transfusion	Comment
1	60	Postthyroidectomy	Profound	Moderate	80/50	500	.....	Good	Tracheotomy and control of hemorrhage; no subsequent blood transfusion necessary
2	31	Postpartum	Extremely profound	60% of total blood	Could not be obtained	1,400	120/80	Excellent	Blood transfusion after serum for anemia
3	35	Placenta praevia; transverse presentation	Profound	Extensive; 5,000+ cc. until hemorrhage was controlled	Could not be obtained	1,000	.....	Shock combated; patient sustained until blood transfusion started	Serum transfusion followed by 4,800 cc. of blood in next 7 hours owing to uncontrollable hemorrhage; hysterectomy after 7 hours; recovery
4	25	Abdominal gun wound	Profound	Extensive	Low	450	.....	Temporarily good	Extensive operation; generalized peritonitis; two blood transfusions; died 24 hours later
5	21	Knife wound in left femoral and profunda arteries, femoral and saphenous veins	Profound	± 40% of total blood	Low	500	.....	Very good	Control of hemorrhage; blood transfusion 3 days later for anemia
6	35	Placenta praevia	Profound	Extensive	60/40	500	120/78	Very good	Cesarean section; blood transfusion during surgery after serum
7	51	Knife wound of maxillary artery and jugular vein	Profound	Extensive	60/40	1,000	140/80	Excellent	2,000 cc. saline dextrose failed to sustain blood pressure; no subsequent blood transfusion necessary
8	25	Postpartum hemorrhage	Profound	Over 1,500 cc.	65/35	700	105/60	Very good	Also given five blood transfusions subsequently in next 3 days; hemorrhage stopped after curettage 3 days later
9	30	Knife wounds of chest, scalp, face and hands; severed arteries	Profound	Extensive	Low	500	120/70	Progressive rapid recovery	No blood transfusion necessary
10	19	Cesarean section	Moderate	300+ cc.	52/40	500	130/70	Good	Surgery; no blood transfusion necessary
11	46	Vaginal hysterectomy	Moderate	600 cc.	70/50	500	.....	Very good	No blood transfusion necessary
12	24	Uterine	Moderate	Extensive	Low	500	.....	Very good	Curettage; serum followed by blood transfusion
13	30	Ruptured ectopic pregnancy	Moderate	400 cc.	78/46	500	108/80	Very good	Salpingectomy; no blood transfusion necessary
14	20	Postpartum	Moderate	600 cc.	Low	500	.....	Very good	Blood transfusion 12 hours later for anemia
15	70	Gastrointestinal (cirrhosis)	Moderate	Extensive	.....	500	.....	Temporarily beneficial	Blood transfusion 3 hours after serum; died 3 days later
16	39	Hysterectomy	Moderate	Moderate	116/56	500	120/60	Very good	Followed by three blood transfusions subsequently for anemia

CASE 1 (chart 1).—A secundigravida-primipara aged 31 was admitted to the service of Dr. Julius Lackner on Feb. 7, 1940, two weeks overdue according to date. The fetal head was overriding and could not be impressed into the pelvis, but x-ray cephalopelvimetry revealed no disproportion. Labor was initiated spontaneously and the patient delivered precipitately after eight hours of tumultuous labor. There was a loss of from 700 to

800 cc. of blood by the completion of the third stage, and intermittent profuse blood loss thereafter despite all effort to keep the uterus contracted.

Although 750 cc. of 10 per cent dextrose in physiologic solution of sodium chloride was administered, the shock became progressively more profound. Human serum transfusion was

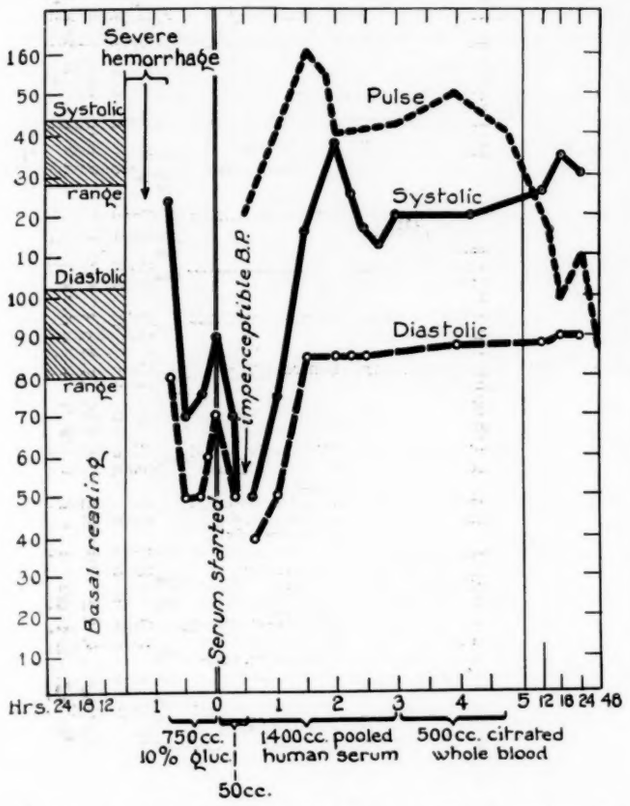

Chart 1 (case 1).—Serum transfusion for obstetric hemorrhage and shock.

started at a time when neither blood pressure nor pulse could be obtained and the patient was moribund. No effect was observed at the outset, and then it was realized that the serum was being given too slowly through a small needle. This was corrected by changing to two large needles, one in each cubital vein, and the serum was infused rapidly. There was a very prompt response to this rapid serum infusion, with a return of blood pressure to 118 systolic, 85 diastolic, when only 700 cc. had been administered. A total of 1,400 cc. of serum was given, after which the patient was conscious, had a blood pressure of 120 systolic, 86 diastolic and a pulse of 140 and of good quality. That the blood loss was extreme is disclosed by the laboratory examinations. On admission the patient's red blood count was 4,900,000, the hemoglobin 80 per cent Tallqvist (equivalent to approximately 13 Gm. Sahli); after the serum transfusion the hemoglobin was only 5 Gm. Sahli. Three hours later, because of the acute anemia, 500 cc. of citrated whole blood was administered. This was followed subsequently by another blood transfusion. The patient had an uncomplicated puerperium.

It is noteworthy that compatibility tests with blood drawn from the patient immediately after the serum transfusion matched perfectly the blood of donors of the same blood group (A). Apparently the isoagglutinins in the pooled serum used for transfusion had been promptly suppressed.

CASE 2 (chart 2).—C. F., aged 51, was admitted to the hospital in the service of Dr. James Patejdl in profound shock with a blood pressure of 60 systolic, 40 diastolic and a weak rapid pulse following hemorrhage due to deep lacerations below the left mandible involving the external maxillary artery and external jugular vein. The bleeding vessels were clamped and 2,000 cc. of 5 per cent dextrose in saline solution was immediately administered. Following this infusion the patient's condition improved and the blood pressure rose to 140 systolic, 80 diastolic. However, within the next hour the patient again lapsed into profound shock, the blood pressure fell to 60 systolic, 40 diastolic, the pulse became weak and barely perceptible and the patient cold, clammy and unconscious.

Another liter of 10 per cent dextrose in saline solution was started and again the condition improved, the blood pressure slowly rising to 105 systolic, 60 diastolic. However, this improvement was likewise only temporary, and it was apparent that the crystalloid solution was ineffective because it was not remaining in the circulation. At this time, when the patient's blood pressure was around 80 systolic, 60 diastolic, 1,000 cc. of pooled human serum was administered. When a little more than half this amount had been given the patient's blood pressure was 120 systolic, 80 diastolic, and at the conclusion of the serum administration the blood pressure was 140 systolic, 80 diastolic. The pulse was of good quality, the rate being between 90 and 100. The general condition was quite good.

The patient continued to improve and no further shock treatment or blood transfusion was necessary.

CASE 3.—B. D., a tertigravida-secundipara aged 35, was admitted to the hospital May 9, 1940, with placenta praevia and a deviated breech presentation. Four hours subsequent to bag insertion contractions started. The fetal heart tones disappeared about five hours later. Seven hours later profuse hemorrhage developed and the patient went into shock. The blood pressure dropped to 75 systolic, 40 diastolic and then could not be obtained. The pulse was rapid and feeble. A serum transfusion was immediately started, and although bleeding continued the shock picture receded and the blood pressure improved. Immediately after transfusion of 1,000 cc. of serum, blood transfusions were started. At the end of seven hours, during which time there was active labor, extraction of a dead fetus, packing of the uterus which was ineffective, application

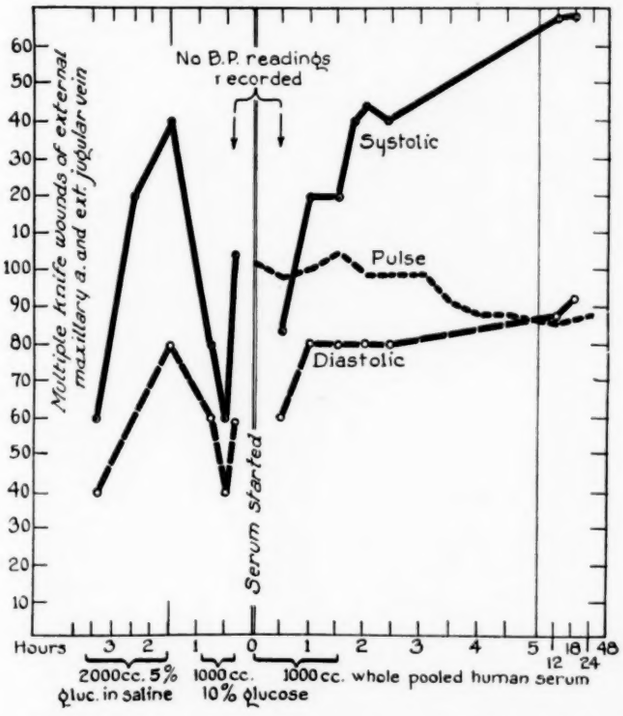
Multiple knife wounds of external maxillary a. and ext. jugular vein
No B.P. readings recorded
Systolic
Pulse
Diastolic
Serum started
Hours 3 2 1 0 1 2 3 4 5 18 12 24 48
2000cc. 5% gluc. in saline
1000cc. 10% glucose
1000cc. whole pooled human serum

Chart 2 (case 2).—Serum transfusions for traumatic hemorrhage and shock; sustained effect following serum, only transient effect from saline-dextrose infusions.

of a Momberg belt and hysterectomy, a total of 4,000 cc. of blood was administered. There was a subsequent temporary paresis of both lower extremities and a complicating bilateral bronchopneumonia.

This case illustrates the interval use of serum followed by blood transfusions. The serum combated shock

and sustained the blood pressure until blood transfusions were started.

It must be pointed out that in these three instances any delay before treatment, even of only fifteen or thirty minutes, might have been fatal. Such delay is unavoidable with the use of whole blood. This is true even when an institution has a blood bank, because before preserved blood can be administered the patient's blood must be typed and a compatibility test performed. Serum is kept on hand in the operating room and in the labor rooms, and no delay is encountered in its administration.

TABLE 2.—*Summary of Results of Serum Transfusion in Other Conditions*

Case	Age, Yrs.	Diagnosis	Indications for Serum	Laboratory Data	Amount of Serum	Response to Serum	Other Treatment	Comment
Shock (not associated with hemorrhage)								
17	44	Carcinoma of rectum	Resection of rectum; operative shock	Blood pressure fell from 130/86 to 50/40	500 cc.	Prompt; progressive rise in blood pressure	Intravenous fluids	Good operative recovery
18	23	Carcinoma of breast	Radical mastectomy; operative shock	.....	500 cc.	Prompt; improved circulation	.....	Good operative recovery
19	4	Congenital dislocation of hip	Open reduction; operative shock	Pulse and blood pressure imperceptible	250 cc.	Prompt; blood pressure rose to 85/55	Intravenous fluids	Delayed recovery; streptococcic septicemia
20	33	Multiple contusions, lacerations and fractured ankle following 45 foot fall	Traumatic shock	.....	400 cc.	Prompt; recovery from shock	General	Uncomplicated recovery
21	21	Acute inversion of uterus	Visceral and operative shock	Blood pressure fell from 150/70 to 65/40	260 cc.	Gradual improvement	Stimulants; blood transfusion and fluids	Uncomplicated puerperium
22	36	Vaginal hysterectomy for menometrorrhagia	"Pituitrin shock" (1 cc. in myometrium)	Pulse and blood pressure imperceptible	400 cc.	Prompt improvement	Blood transfusion and dextrose intravenously	Uncomplicated recovery
23	29	Term pregnancy; previous classic cesarean section	"Pituitrin shock" (1 cc. in myometrium)	Pulse and blood pressure imperceptible	500 cc.	Prompt recovery, although improvement noted when serum started	Blood transfusion 4 days later	Uncomplicated recovery
Hypoproteinemia								
24	49	Starvation due to cardiospasm with nutritional edema and polyavitaminosis	Inadequate oral protein intake	Serum protein 3.8 Serum albumin 2.6 Serum globulin 1.2	110 cc. (4 × concentrated) 100 cc. (4 × concentrated)	Rise of serum proteins to 5.7 with diuresis and weight loss	Parenteral vitamin therapy; general supportive, antispasmodics	Gradual recovery
25	2½	Nephrosis	Low blood protein and marked albuminuria	.....	500 cc. in 5 divided amounts	Questionable	Diuretics; general supportive	Improved
26	52	Acute and chronic hepatitis	Edema; low blood protein	Serum protein 5.5 Serum albumin 2.3 Serum globulin 3.2	1,500 cc. (divided doses over 2 weeks)	Temporary improvement	Blood transfusions; supportive, dextrose intravenously	Died; no reaction
27	43	(Idiopathic ?) embolic occlusion of right iliac artery	Prolonged septic course; low serum protein and generalized edema	Serum protein 5.5 Serum albumin 2.6 Serum globulin 2.9	500 cc.	Increased urinary output and diminished edema	Amputation following embolectomy; 4 (500 cc.) blood transfusions	Eventual recovery
28	1½	Ruptured appendix and generalized peritonitis	Protein loss from draining wound	.....	250 cc. (2 ×)	Cannot evaluate	Surgery; blood transfusions	Died 2 weeks postoperatively; no reaction
29	66	Gastro-enterostomy for old duodenal adhesions (postoperative)	Very low blood protein	Serum protein varied from 4 to 5.8	5,000 cc. (over 24 days)	Cannot evaluate	2,000 cc. blood (over 24 days)	Died; general peritonitis, bronchopneumonia; no reaction
30	2	Nephrosis	Low blood protein; albuminuria	Serum protein 4.3-4.8	Varying amounts of human serum; 4 × concentrated serum; human plasma	Increased urinary output; diminished edema	Diuretics, supportive	Response to whole serum equal to any other therapy; no response when febrile; no reaction
Burns								
31	5	2d-3d degree burns of 30 per cent of body surface	Plasma loss; shock	.....	100 cc. (4 × concentrated) and repeated	Good	Blood transfusions; gentian silver nitrate spray to burn; fluids	Prolonged septic course; good recovery; no reactions
32	27	2d-3d degree burns of 75 per cent of body surface	Plasma loss; shock	.....	100 cc. (4 × concentrated) 2 ×	Cannot evaluate	Tannic silver nitrate spray; two blood transfusions; fluids	Complicating bronchopneumonia; died; no reactions
33	17	2d-3d degree burns of 60 per cent of body surface	Plasma loss; shock	.....	1,000 cc. many hours later	Cannot evaluate	.....	Died within 24 hours; no serum reactions

SHOCK NOT ASSOCIATED WITH HEMORRHAGE

The group of shock not associated with hemorrhage comprises seven cases, four associated with surgical procedures, two following the administration of solution of posterior pituitary injected into the myometrium during surgery and one due to trauma (table 2). In all instances the patients who had every clinical evidence of shock promptly responded to the serum transfusion with a rise in blood pressure, slower and fuller pulse and improvement in the general condition.

CASE 4 (chart 3).—F. B., a secundigravida-secundipara aged 29, in the service of Dr. Julius Lackner, had had a classic cesarean section performed for complete abruptio placentae in 1936. On Feb. 20, 1940, a low cervical cesarean section was performed. After extraction of the baby 1 cc. of solution of posterior pituitary was injected into the myometrium in order to control the somewhat excessive bleeding. Within a few minutes the blood pressure and pulse became imperceptible. Two hundred and fifty cc. of physiologic solution of sodium chloride was administered, from which there was no apparent beneficial effect. Then 500 cc. of pooled human serum was injected. Following this the blood pressure was 102 systolic, 50 diastolic and the pulse 140 and of good quality. The blood pressure continued to rise and one hour later was 130 systolic, 90 diastolic. On the fourth postoperative day 500 cc. of citrated blood was given, following which a generalized urticaria developed. This was relieved by epinephrine. On the tenth postoperative day 0.1 cc. of dilute solution of posterior pituitary was injected intradermally; a marked erythematous pseudopodial reaction followed.

We are aware that most patients recover spontaneously from "pituitrin shock." However, it is a sound surgical principle to institute measures to combat shock when it develops from any cause. This case is particularly interesting since an allergic reaction to whole

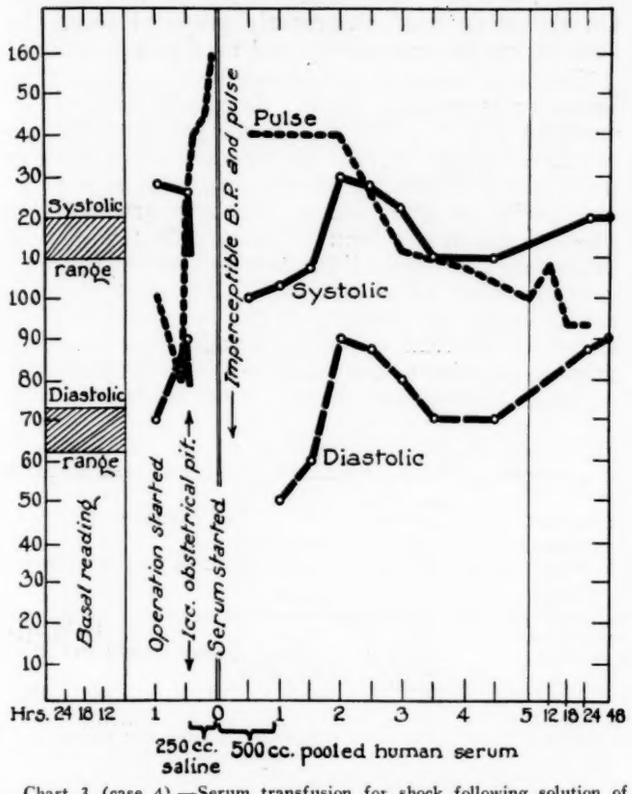

Chart 3 (case 4).—Serum transfusion for shock following solution of posterior pituitary during cesarean section.

blood developed, whereas there was no reaction to the serum infusion.

These patients were not in as critical a condition as those in the hemorrhage and shock group, and it is probable that recovery would have occurred without serum transfusion. However, at the time these patients were in shock restorative measures were deemed necessary.

HYPOPROTEINEMIA

Seven patients received serum transfusions for the treatment of hypoproteinemia. In two cases this condition was associated with nephrosis in children, and the effects of serum transfusions were variable (table 2). In three instances hypoproteinemia was associated with septicemia, and serum transfusion apparently was beneficial although in two the course was ultimately fatal. In one instance the hypoproteinemia was associated with extensive damage of the liver and kidneys, and here likewise serum transfusion seemed of temporary benefit. Case 5, reported briefly, is of particular interest.

CASE 5 (chart 4).—P. DeV., a woman aged 49, in the service of Dr. I. I. Ritter, had suffered from "stomach trouble" for from fifteen to eighteen years. She had not sought medical advice and for the past two or three years had existed entirely on cream soup, broth, custard, jello and coca-cola. Examination and extensive study established the following diagnosis: cardiospasm with esophageal dilatation; starvation with profound nutritional edema; polyavitaminosis, particularly B and C, and hypoproteinemia.

Treatment consisted of a high caloric diet, large amounts of vitamin preparations administered orally and parenterally, and antispasmodics. Oral protein intake was very limited owing to the cardiospasm, and the serum proteins remained low. Therefore 100 cc. of four times concentrated (lyophile) serum, equivalent to 400 cc. of normal serum, was administered twice for the hypoproteinemia. Chart 4 shows the curves of the blood protein values, urinary output and weight with this treatment. It is seen that following the second injection of concentrated serum the blood proteins rose markedly, and there was a concomitant diuresis and resultant loss of weight. This patient was discharged markedly improved.

BURNS

Three patients suffering from burns of the body were treated with serum transfusion (table 2). Two of the patients suffered very severe and extensive burns involving approximately 75 per cent of the body surface, and both patients died. The third patient, who was admitted to the hospital following severe burns of approximately 30 per cent of the body surface, received both serum and blood transfusions and ultimately recovered, despite a prolonged septic course resulting from infection of the burned areas.

We feel that serum transfusions will prove a valuable adjunct in the treatment of severe burns. Our experience is limited at present, but it is reasonable that the plasma loss and hemoconcentration can best be overcome by serum replacement therapy.

MISCELLANEOUS

Fourteen patients were treated for a variety of conditions: cachexia due to infection, hemorrhage and shock with purpura haemorrhagica, exfoliative dermatitis, pneumonia, acute catarrhal jaundice, generalized septicemia and chronic blood loss (table 3). No definite conclusions could be reached as to the value of serum transfusion in these cases because none of them were carefully studied and the serum transfusion was employed as a supportive measure. One case deserves more than passing mention:

A child aged 9 years with septic mastoiditis could be given no blood transfusion owing to universal incompatibility, possibly resulting from intensive sulfanilamide therapy.[4] Serum transfusion was employed as an alternative measure, although blood would have been preferable because of the profound anemia associated with the infection. However, the child was definitely benefited by the serum transfusion, and after the infection was controlled the patient made an uneventful recovery.

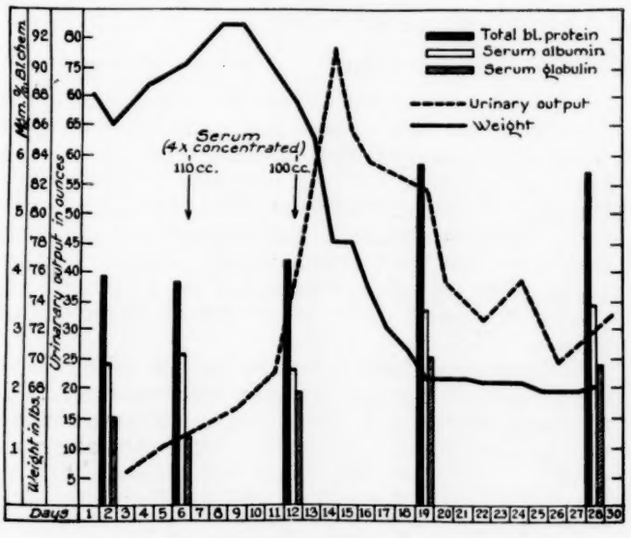

Chart 4 (case 5).—Serum transfusion for hypoproteinemia.

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COMMENT

Serum transfusion as a blood substitute has been mentioned in the past.[5] No practical use was made of this proposal until very recently. Brief reports [6] have pointed out the merit of serum or plasma as a blood substitute. Our experience in the cases observed and reported in this paper completely confirms the evidence brought out in animal experiments [7] that serum is an adequate blood substitute in shock. It appears that serum is an effective agent in many conditions in which blood transfusion would ordinarily be employed, with the exception of those conditions in which extensive loss of red blood cells occurs. Even in acute hemorrhage serum is a valuable temporary and intermediate treatment until blood can be secured, since it maintains circulating volume, thereby sustaining blood pressure and combating shock, anoxia and acidosis. The advantages of serum have previously been enumerated but can be summed up in the statement that serum can be prepared in very large amounts, can be stored over a long period of time without deteriorating and sided subsequently. No reaction of a pyrogenic nature or blood group incompatibility was observed.

It is important to point out that the preparation of serum requires scrupulous care and meticulous technic. Many reports [10] on serum prepared by trained personnel affirm the safety and innocuousness of this material. On the other hand, improperly prepared serum has been known to cause severe and even fatal reactions.[11]

There are no great differences between plasma and serum as transfusion fluids. Essentially, freshly prepared plasma is serum plus fibrinogen, thrombin and one fifth dilution with 2.5 per cent sodium citrate solution. In our experience plasma cannot be kept over a long period of time because fibrinogen gradually precipitates out in the form of fibrin veils and granular precipitate and requires filtration or centrifugation and clearing before administration. After most or all of the fibrinogen has precipitated out, the solution consists essentially of serum diluted with sodium citrate. If the original intention of the laboratory is to prepare either serum or plasma, we believe that the former is preferable because after its preparation and clarification by filtration it can be stored indefinitely, retaining its clear state. However, if a laboratory employs the plasma from outdated preserved blood, the supernatant plasma can be withdrawn and if not used within a short time it can subsequently be filtered to remove the fibrin precipitates and then stored for a long period of time. Adequate sterility tests must be performed whenever cloudy plasma is employed.

TABLE 3.—*Summary of Miscellaneous Cases Treated by Serum Transfusion*

Case	Age, Years	Clinical Diagnosis	Indication for Serum	Amount of Serum	Comment
34	10	Acute catarrhal hepatitis	General supportive regimen	250 cc.	Recovered
35	13	Banti's syndrome, pneumococcemia, amebic dysentery	Generalized edema; ascites	500 cc.	Death; necropsy; Laënnec's cirrhosis
36	4	Influenzal meningitis	General supportive regimen	250 cc.	Death
37	9	Otogenic sepsis	Universal blood incompatibility	250 cc.	Progressive recovery
38	49	Streptococcic lobar pneumonia	Nonspecific supportive therapy	500 cc.	Death
39	48	Severe exfoliative dermatitis (etiology ?)	Marked toxicity; cachexia	1,550 cc. in divided amounts over 2 mos.	Temporary improvement; died after 5 months
40	54	Ulcerative colitis	Cachexia; general supportive	250 cc.	.....
41	54	Gastric ulcer with obstruction; subtotal gastrectomy	Postoperative supportive treatment	500 cc.	Temporarily improved; complicating pneumonia; death eighth postoperative day
42	32	Thrombocytopenic purpura; intracranial hemorrhage	Moribund	700 cc.	Death
43	47	Peptic ulcer with hemorrhage; heart failure	Elevated nonprotein nitrogen; cachexia	500 cc.	Temporary clinical improvement; subsequent death
44	?	Hypertensive encephalopathy	Inadequate protein intake	250 cc.	.....
45	58	Carcinoma of rectum; abdominoperineal resection	General supportive; cachexia	500 cc.	Extensive necrosis of abdominal wall; progressive recovery
46	4	Medulloblastoma of cerebellum	Cachexia	400 cc.	Death
47	42	Generalized peritonitis following ruptured appendix	Postoperative cachexia; blood transfusion reactions	2,000 cc. over 7 days	Improved; reaction to serum consisting of immediate pain, burning, swelling and redness along course of vein

can be shipped and handled easily. A factor of utmost importance is that serum transfusion can be given without preliminary typing and compatibility tests. The latter consideration has been discussed in a recent publication [8] in which it is shown that agglutinogen in the patient's serum absorbs infused agglutinins and inhibits their action on the patient's red blood cells. Furthermore, a low agglutinin titer serum can be prepared by pooling a large number of serums of varying blood groups.

Objection has been raised to the use of serum on the grounds that severe reactions are encountered.[9] In the cases reported here, a reaction was observed in only one instance. This consisted of local pain along the course of the vein into which the serum was being injected, followed by redness and swelling which subsided subsequently.

Flasks of serum are now being stored in labor rooms, operating rooms and first aid stations for immediate use in obstetric and surgical emergencies. The use of serum will increase the efficiency and adaptability of any hospital blood transfusion service, and outdated preserved blood need not be discarded. In the light of the foregoing discussion it is unnecessary to point out the great advantages of serum in the medical military service.

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SUMMARY

1. Forty-seven patients suffering from a variety of conditions received human serum transfusions.

2. Patients suffering with shock from hemorrhage and other causes, hypoproteinemia or burns were definitely benefited by serum transfusion, and in a number of instances a dramatic recovery was observed.

3. The supply of serum is limited only by the supply of blood, and once it is prepared it can be preserved for a long time.

4. Serum transfusions may be given without preliminary laboratory typing and compatibility tests.

5. No reactions were observed or need be anticipated if serum is properly prepared. However, meticulous care must be taken in the preparation of serum.

6. Serum is preferred to plasma because it does not contain sodium citrate and because fibrin precipitates do not occur.

7. Serum is a valuable adjunct to any hospital or military transfusion service.

Twenty-Ninth Street and Ellis Avenue.

ABSTRACT OF DISCUSSION

DR. JOSEPH A. WAGNER, Bryn Mawr, Pa.: In our experience at the Bryn Mawr Hospital, reactions frequently follow the intravenous use of serum. Serum is the liquid phase of the blood separated after clotting has taken place, whereas plasma is the liquid phase of the blood separated without clotting. There are profound differences between the two substances which have been brought out in a number of ways. These may be grouped as follows: First, reactions following administration of fresh serum or serum preserved by drying from the frozen state. These have been reported in animals by Ravdin, Levinson and Freedman and their co-workers and in man by Aldrich, Ravdin and their co-workers and by Strumia and me. On the other hand, plasma fresh or preserved by either refrigeration or drying from the frozen state has now been widely employed by a number of experimenters in animals without reaction and clinically by Elliott, Lehman, Saint Girons, Ravdin, Knott, Edwards and others and by our own group. We have had experience with the material for at least eleven years, during which time more than 1,200 intravenous administrations have been given under closely controlled conditions and in doses as large as 2,000 cc. in twenty-four hours without disturbance. As much as 9 liters was given to one patient in eleven days. When one compares the electrophoretic pattern of serum and plasma as determined by the Titelius apparatus by Dr. Scudder, gross differences are at once appreciated. The cutaneous reactivity of animals and man to minute intradermal doses of serum and plasma offers a striking difference. When plasma is administered subcutaneously or intramuscularly, the rate of absorption is comparable to that of physiologic solution of sodium chloride. When serum is injected the rate of absorption is much slower. All these arguments point to a profound difference between serum and plasma and suggest, as Brodie first observed in 1900, that in the process of clotting a change is brought about in the serum which makes it toxic. Plasma has other advantages besides that of complete freedom from reaction. It is first of all more readily obtained than serum; second, it gives a greater yield of the liquid phase; finally, in the institutions where blood banks are established it is a readily obtained by-product. While we agree that on the whole physiologic effect of fresh serum is comparable to that of plasma in the treatment of shock, the fact that plasma has mechanical advantages in separation and freedom from reactions when administered intravenously makes it the material of choice.

DR. SIDNEY O. LEVINSON, Chicago: It is surprising that the discussion does not involve the validity of the claim that human serum is a good substitute but rather focuses around the question of whether serum or plasma is superior. Such controversy appears relatively unimportant, because both answer the purpose of supplying a human colloid protein-containing fluid. I hold no brief for either serum or plasma. Where the latter is more easily available and prepared (as in blood banks), plasma should be used; where the former can be properly and easily handled, serum is to be preferred. I protest emphatically that properly prepared serum is not toxic. Human serum has been used extensively in Illinois by thousands of physicians in the last ten years, and with the exception of occasional allergic reactions no ill effect has been experienced or reported. Toxic reactions, such as those reported by Dr. Strumia, have been conspicuous by their absence. The handling of clotted blood is different from that of citrated blood. The unfavorable laboratory and clinical results reported may well be due to the use of technic different from that employed successfully by the various serum centers throughout the country. Wide experience from all serum centers indicates that properly prepared serum is safe. I have no doubt that if plasma was improperly prepared it would not be innocuous. We are all aware of the fact that even a simple material like saline solution may cause severe reactions. Technic and care in preparation are of the greatest importance. In all other matters I agree with Dr. Wagner. Either serum or plasma, having the same essential properties, may be used to great advantage and with complete safety.

REDUCTION OF ELEVATED BLOOD PRESSURE BY ADMINISTRATION OF RENAL EXTRACTS

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A number of investigators have claimed beneficial results from the administration of renal extract. The earliest studies were those of Brown-Séquard and d'Arsonval [1] in 1892 and of Meyer [2] the following year. These authors reported that nephrectomized animals were improved by their crude extracts. More recently it has been stated [3] that renal venous blood contains a substance which in animals causes diuresis, with reduction in the amount of sodium, chloride, potassium and urea in the blood. It has likewise been claimed [4] that extracts of the kidney cause diuresis and reduction of blood pressure in patients with nephritis. These therapeutic claims have not been confirmed nor have they received any serious consideration by competent authorities for a number of reasons. In the first place the hypotensive action claimed for these extracts has not been demonstrated in hypertensive animals. Secondly, the clinical data have not been convincing. In most instances only one measurement of blood pressure has been reported prior to the administration of the renal extract. Since it is well known that striking variations in blood pressure occur in hypertensive subjects and since it is generally recognized that such patients usually have a higher blood pressure when first observed by a physician than when subsequently seen by the same

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Read before the joint meeting of the Section on Practice of Medicine and the Section on Pharmacology and Therapeutics at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Brown-Séquard and d'Arsonval: Compt. rend. Acad. d. sc. **114:** 400, 1892.

2. Meyer, E.: Arch. de physiol. norm. et path., 1893, p. 760; 1894, p. 179.

3. Tokumitsu, Y.: Folia endocrin. Japon., Tr. Jap. Path. Soc. **24:** 444, 1934.

4. Gomez, D. M.: Compt. rend. Soc. de biol. **116:** 876, 1934; Presse méd. **42:** 1371 (Sept. 1) 1934; **43:** 219 (Feb. 9) 1935. Jablons.[5]

physician, critical readers have naturally been inclined to regard the diminution in blood pressure reported as of spontaneous origin rather than as due to the therapy. A third and especially important reason for the skepticism which has existed concerning the hypotensive and other therapeutic actions claimed for renal extracts has been the lack of any convincing rationale for their use. It is difficult to reconcile the reported effects of renal extracts [5] on excretion with the current concepts of renal function. On the other hand, there is much recent evidence which points to the kidney as the organ most frequently responsible for hypertension and which suggests that such hypertension is related to a disturbance in the formation of certain substances in the kidney.[6]

RATIONALE FOR THE USE OF RENAL EXTRACT IN THE TREATMENT OF HYPERTENSION

Until comparatively recently it was generally believed that most instances of hypertension were due to disease originating in some part of the body other than the kidney. In cases of glomerular nephritis, in which the renal origin of the hypertension was conceded, it was thought that the increase in blood pressure was brought about by the failure of the kidney to excrete some pressor substance. The validity of the first of these conceptions was made questionable when Goldblatt, Lynch, Hanzal and Summerville [7] showed that constriction of the renal arteries produced hypertension in dogs but that such animals often presented a clinical picture resembling in most respects that of patients with the so-called essential (i. e., nonrenal) hypertension. Since a well marked elevation of blood pressure was shown to exist in the absence of accumulation in the blood of any of the known and measurable excretory products, the validity of the excretory failure theory of renal hypertension was naturally questioned. Further doubt as to the correctness of this concept was furnished by the experiments of Harrison, Mason, Resnik and Rainey,[8] who showed that, whereas bilateral nephrectomy induced no rise in blood pressure, ligation of both ureters caused a slight but definite elevation of pressure in most of the experimental animals. This observation led to the conclusion that renal hypertension was not due to the failure of the kidney to excrete some hypothetical pressor substance but was dependent on the presence in the body of abnormally functioning renal tissue. It was then shown by several different groups of investigators that renal hypertension could not be abolished by denervation of the kidney, and this demonstration seemed to establish the importance of a humoral rather than a nervous mechanism. That kidney extracts contain a pressor substance has been known for nearly forty years, since the original experiments of Tigerstedt and Bergman,[9] in which renin was described. We are not concerned here with the disputed question as to whether renin is actually the effective pressor agent inducing hypertension. Evidence bearing on this question has recently been summarized elsewhere by Page [10] and by ourselves.[11] What we are concerned with is the fact that evidence derived from the studies of the effects of renin has led to the development of a logical basis for the idea that extracts of the kidneys might be of value in the treatment of hypertension due to renal disorders. The evidence for this proposition may be briefly summarized as follows:

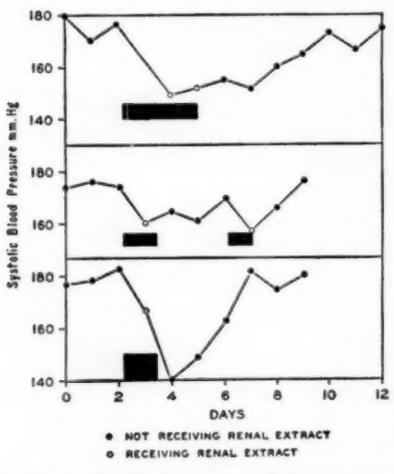


Chart 1.—Three different experiments, each involving the use of four hypertensive rats. The first experiment shows the effect of feeding the renal extract in a rather small dose over a period of several days. The second or middle curve depicts the effect of administering small amounts of the extract for one day only on two separate occasions. The third or lowest curve illustrates the result obtained when a relatively large amount of the active principle was administered for a short period of time. In all instances the decline in blood pressure came on slowly and did not disappear for several days after the extract had been discontinued.

In their original publication Tigerstedt and Bergman [9] pointed out that renin induced a greater rise in blood pressure in nephrectomized than in normal animals. They attributed this difference to failure of the nephrectomized animals to excrete the pressor substance. In repeating their experiments Merrill, Williams and Harrison [12] noted that the increase in sensitivity did not appear immediately after nephrectomy but only after a number of hours had elapsed. This led these authors to suspect that normal renal tissue might form some substance which was distributed in the body and which had the property of limiting the pressor effect of renin. This increased sensitivity of nephrectomized animals to the renal pressor substance has also been observed by other investigators, including Leiter and Eichelberger,[13] Page [14] and Freedman.[15]

Further indirect evidence for the existence of a renal antipressor substance was furnished by the experiments of Blalock and Levy,[16] who showed that in an animal with unilateral ischemia removal of the normal kidney resulted in a marked rise in blood pressure. The observation of Katz, Rodbard, Steinitz and Friedberg,[17] which indicated that renal hypertension is dependent on the ratio of ischemic to normal kidney tissue, was compatible also with the hypothesis of the elaboration of an antipressor principle by the normal kidney.

5. Jablons, Benjamin: New York State J. Med. **38:** 31 (Jan. 1) 1938. Tokomitsu.[3] Gomez.[4]

6. In the foregoing discussion, extracts from organs other than the kidneys have not been discussed. It should be mentioned, however, that a number of observers have found in urine substances having a well marked depressor action. Thus, Abelous and Bardier (Compt. rend. Soc. de biol. **66:** 88, 347, 1909) described "urohypotensin," Frey and Kraut (Arch. f. exper. Path. u. Pharmakol. **133:** 1, 1928. Frey: München. med. Wchnschr. **76:** 1951 [Nov. 22] 1929) "kallikrein," and Wollheim and Lange (Deutsche med. Wchnschr. **58:** 572 [April 8] 1932. Wollheim: Acta med. Scandinav. **91:** 1, 1937) found "depressan" ("detonin"). All of these substances could be precipitated by alcohol and by ammonium sulfate and were nondialyzable. However, kallikrein was heat labile, while urohypotensin and depressan (which are possibly identical substances) resist boiling. Of particular interest is the report that depressan is present in the urine of persons with normal blood pressure and of patients with renal hypertension but is absent or markedly diminished in the urine of persons with "essential" hypertension. In the latter subjects Wollheim found diminution in the blood pressure following the intramuscular administration of depressan. Space does not permit a detailed discussion of depressor extracts of tissues other than kidney. Certain properties of these substances will be summarized in the accompanying table.

7. Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: J. Exper. Med. **59:** 347 (March) 1934.

8. Harrison, T. R.; Mason, M. F.; Resnik, Harry, and Rainey, J.: Tr. A. Amer. Physicians **51:** 280, 1936.

9 Tigerstedt, R., and Bergman, P. G.: Skandinav. Arch. f. Physiol. **8:** 223, 1898.

10. Page, I. H.: J. Exper. Med. **70:** 521 (Nov.) 1939.

11. Williams, J. R., Jr.; Grollman, Arthur, and Harrison, T. R., to be published.

12. Merrill, Arthur; Williams, J. R., Jr., and Harrison, T. R.: Am. J. M. Sc. **196:** 240 (Aug.) 1938.

13. Leiter, L., and Eichelberger, L.: Proc. Soc. Clin. Investigation **18:** 477, 1939.

14. Page, Irvine: Personal communication to the authors.

15. Freedman, Arthur: Am. Heart J., to be published.

16. Blalock, Alfred, and Levy, S. E.: Ann. Surg. **106:** 826 (Nov.) 1937.

17. Katz, L. N.; Rodbard, S; Steinitz, F. S., and Friedberg, L.: Proc. Soc. Clin. Investigation **18:** 480, 1939.

Additional support for the hypothesis of an antipressor substance was furnished by experiments in which it was shown that extracts of normal kidneys tended on standing to lose their pressor property more rapidly than did similarly prepared extracts of ischemic kidney of the same animal.[11]

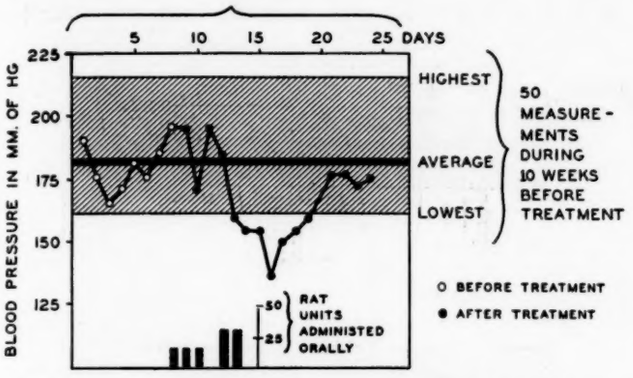


Chart 2.—The administration of 15 rat units a day for three days to this dog had practically no effect on the blood pressure. When the dose was doubled, a definite decline in pressure occurred which persisted for several days after the administration of the extract had been discontinued.

Perhaps the most convincing indirect evidence for the existence of a humoral antipressor substance is the observation that hypertensive pregnant animals commonly develop a well marked decline in blood pressure during the last part of pregnancy and that the blood pressure increases to its previously elevated level following delivery.[18] It is difficult to account for such a sequence of events except by assuming that the fetus or the placenta forms some substance capable of reducing the elevated blood pressure of the maternal organism.

The observations which have been cited all suggest that the kidneys elaborate some substance which has the property of inhibiting the pressor effect of certain

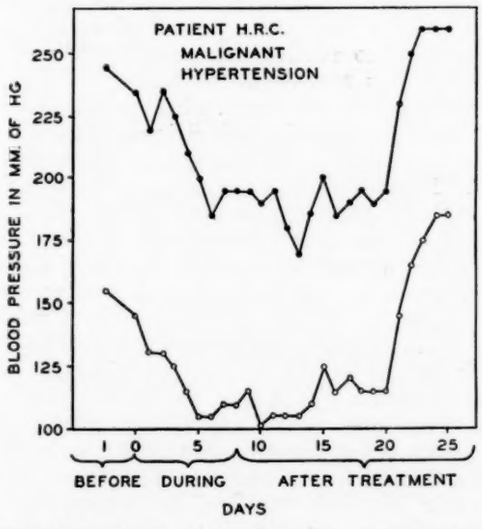


Chart 3.—The decline in blood pressure set in slowly and was not striking until the patient had received the extract for several days. After the medication was discontinued the blood pressure remained at a relatively low level for more than a week and then rapidly rose to the previous elevated level.

agents, including the renal pressor substance renin. Direct evidence of the validity of this hypothesis was obtained when it was found that extracts prepared from the kidneys of various animals did diminish the sensitivity of rats to renin and certain other pressor substances.[18] The next problem investigated was whether extracts containing this antipressor substance would affect the blood pressure of animals with renal hypertension.[19]

EFFECT OF ADMINISTRATION OF RENAL ANTIPRESSOR SUBSTANCE ON BLOOD PRESSURE OF ANIMALS WITH EXPERIMENTAL RENAL HYPERTENSION

In order to conduct any comprehensive study which involves bio-assays, a convenient test object is necessary. The rat seemed ideal for this purpose because of the economic advantages of using small animals in work requiring large numbers of animals. However, in order to test the effect of extracts it was necessary that a satisfactory method of measuring blood pressure without anesthesia be developed. Such a method involving the enclosure of the distal portion of the tail in a plethysmograph was evolved.[20] Accordingly a study was made of renal extracts prepared by various methods and administered to rats rendered hypertensive by subtotal nephrectomy.[18] In the first experiments parenteral administration was employed, but after it was found that oral administration was also efficacious

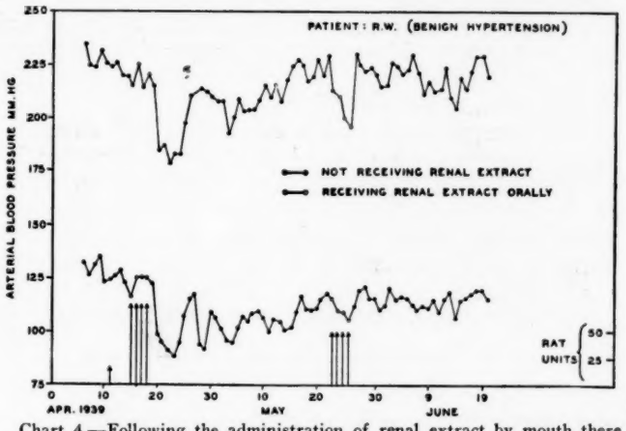


Chart 4.—Following the administration of renal extract by mouth there was a moderate decline in both the systolic and the diastolic blood pressure. This decline persisted for several days after the extract had been discontinued. The blood pressure then rose to the previous level. A month later the administration of the extract in somewhat smaller doses was attended with a less striking decline in blood pressure.

this route has been mainly used, even though larger amounts of material are required.

Typical examples of experiments in which renal extracts having an antipressor action were administered orally—by admixture with the food—to hypertensive rats are illustrated in chart 1. The decline in blood pressure sets in slowly and lasts for a number of days after the animals have resumed their normal diet. It was soon learned that markedly hypertensive rats frequently appeared ill and occasionally died following a rapid decline of their blood pressure. At present it is uncertain whether such deleterious effects are due to impurities or to lowering of the blood pressure per se.

Having repeated the observations on rats in several hundred different experiments and having shown that adequate amounts of properly prepared renal extract would regularly induce a fall in blood pressure, we next investigated dogs with hypertension due to renal ischemia. Here again a decline in blood pressure

18. Harrison, T. R.;; Grollman, Arthur, and Williams, J. R., Jr.: Am. J. Physiol. **128:** 716 (March) 1940.

19. Although the extracts that we have used have produced diminished sensitivity to renin in normal animals and have caused decline in blood pressure in hypertensive animals, it does not necessarily follow that these two effects are due to the same substance. No such conclusion can be justifiably drawn until a high degree of purification of the extracts has been accomplished.

20. Williams, J. R., Jr.; Grollman, Arthur, and Harrison, T. R.: J. Clin. Investigation **18:** 373 (May) 1939.

occurred in most of the experiments.[21] The fact that in an occasional dog no reduction of blood pressure was observed was readily accounted for when the quantity of the active principle administered as determined by assays on rats was taken into account. It was found that from thirty to fifty times as much material had to be given to dogs in order to induce the same decline in blood pressure as occurred in rats. In the initial stages of our work it was difficult to produce sufficient of the extract to treat such a large animal as the dog, and it was often difficult to persuade the animal to ingest it. Vomiting occurred frequently after the administration of the preparation by stomach tube. In the dog as in the rat, toxic effects were frequently observed. These appeared to be of two types. In some animals no untoward effect appeared following a reduction of from 20 to 40 mm. in blood pressure. However, in other animals, and especially in those with marked hypertension of long duration, a drastic decline in blood pressure was accompanied by manifestations of uremia and even by death. In a third group of dogs, which were given relatively small amounts of the active principle as determined by assays on rats, untoward effects occurred without any decline in blood pressure. These effects, which were evidently due to the impurities in the extract, consisted in vomiting, weakness and usually diarrhea. More detailed discussion of the effects of these renal extracts in hypertensive animals have been published elsewhere.[22]

The foregoing discussion concerning the effects of renal extracts on the blood pressure of hypertensive animals may be summarized by saying that it seems to be established beyond question that animals with experimental renal hypertension respond to such extracts with a decline in blood pressure. However, the question as to whether such a decline is in fact desirable or undesirable has not yet been clearly proved.

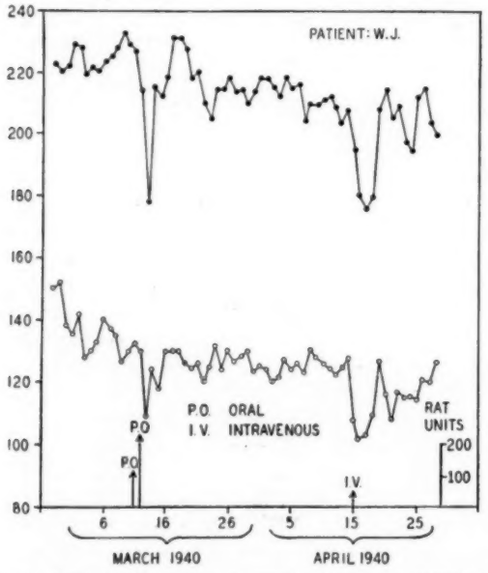


Chart 5.—Oral administration of renal extract was attended by a well marked decline in blood pressure, the effect being of short duration, lasting only for two or three days. On a later date a small dose of renal extract was administered intravenously and a decline of blood pressure of about 30 mm., lasting for about three days, occurred.

For this reason, attempts to treat human beings have naturally had to be carried out slowly and with the greatest caution.

21. Williams, J. R., Jr.; Grollman, Arthur, and Harrison, T. R.: Am. J. Physiol., to be published.
22. Harrison, Grollman and Williams.[18] Williams, Grollman and Harrison.[21]

OBSERVATIONS CONCERNING EFFECTS OF ADMINISTRATION OF RENAL ANTIPRESSOR SUBSTANCE TO PATIENTS WITH HYPERTENSION

Thus far our observations on patients have been limited to subjects with advanced and severe hypertension. The first patients treated were given amounts of extract which we now know to have been far too

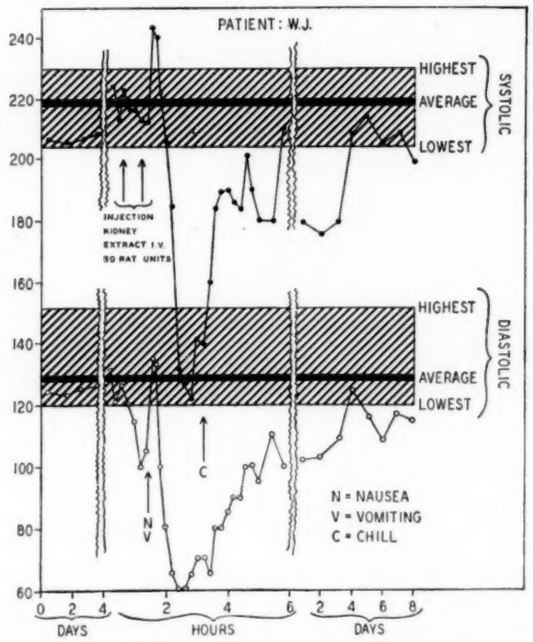


Chart 6.—This illustrates the immediate effects of the intravenous administration of renal extract. The marked decline in blood pressure which came on about two hours after the injection and was followed by a chill possibly represented a nonspecific protein reaction. The more lasting moderate decline was possibly due to the specific effect of the renal extract.

small to have any marked effect. We have treated only a few patients with an amount which would seem adequate, as judged by assays on rats, namely 150 or more oral units a day for a period of several days. The first patient to receive the extract orally in adequate amount was treated in November 1938. This man had malignant hypertension with beginning uremia. He had chronic prostatitis with urinary retention and was therefore catheterized throughout the course of treatment. Because he was desperately ill, the extract was begun on his third day in the hospital. The blood pressure was measured at intervals of every four hours, all of the measurements for a given day being averaged and recorded as one point in chart 3. After several days' treatment a marked decline in blood pressure occurred. About the same time definite clinical improvement with decline in the nonprotein nitrogen of the blood was observed. However, the latter effects may well have been due to the effects of catheterization. As soon as the blood pressure displayed a well marked decline, the treatment was stopped. The blood pressure remained at a relatively low level for several days and then rose to the preexisting value, the patient's symptoms becoming worse. Shortly afterward pneumonia developed and the patient died.

The second patient given adequate amounts of the extract was treated in April 1939. In this case the level of the blood pressure had been studied carefully for a period of several weeks in the hospital a number of months before. After an additional admission to the hospital and a week's control period the administration of the extract was begun with apparently gratifying results on the blood pressure and on the headaches.

After several weeks the blood pressure had gradually risen to the pretreatment level and the extract was again administered orally with an apparent decline in presure (chart 4).

Results on another patient are illustrated in charts 5 and 6. This patient was given a total of about 200 rat units in forty-eight hours. The extracts then had to be discontinued because of diarrhea, which was accompanied by some nausea and vomiting. These symptoms were due we believe to impurities in the extract. This patient exhibited a well marked decline in blood pressure, which lasted, however, for only about twenty-four hours, the pressure then returning to the preexisting level. In order to determine whether the decline in blood pressure could be accounted for solely on the basis of the diarrhea, the patient was later given an amount of magnesium sulfate sufficient to produce a diarrhea approximately as severe as that which occurred during the administration of renal extract. No significant decline in blood pressure occurred. This patient was later given additional renal extract intravenously and a second decline in blood pressure occurred. The possibility that this may have been due to a nonspecific protein reaction has not been eliminated.

In one patient treated orally no decrease in blood pressure was observed even though the patient received what appeared to be adequate amounts of extract during a period of several days. The blood pressure curve of this patient is shown in chart 7.

Observations made during August 1939 on a fifth patient are illustrated in chart 8. This man had severe and advanced malignant hypertension. Prior to the administration of renal extract he was in a state of stupor, was disoriented and had severe headaches which had failed to respond to the usual methods of treatment. During the administration of the renal extract a slow decline in the blood pressure occurred, and this persisted for a number of days after the therapy was discontinued. Coincident with the decline in blood pressure there was marked improvement in the mental

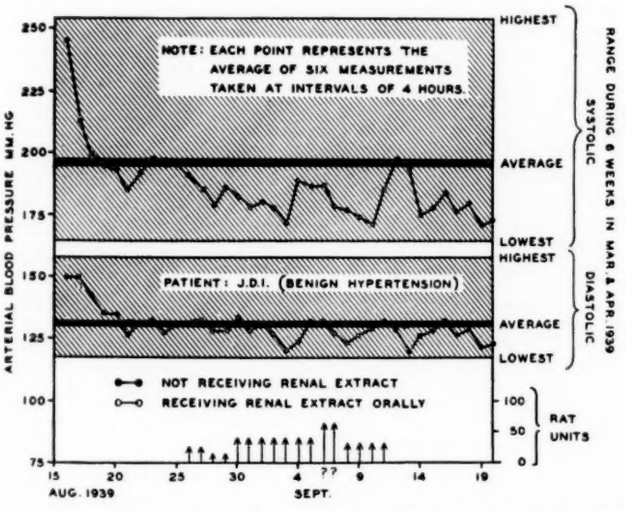
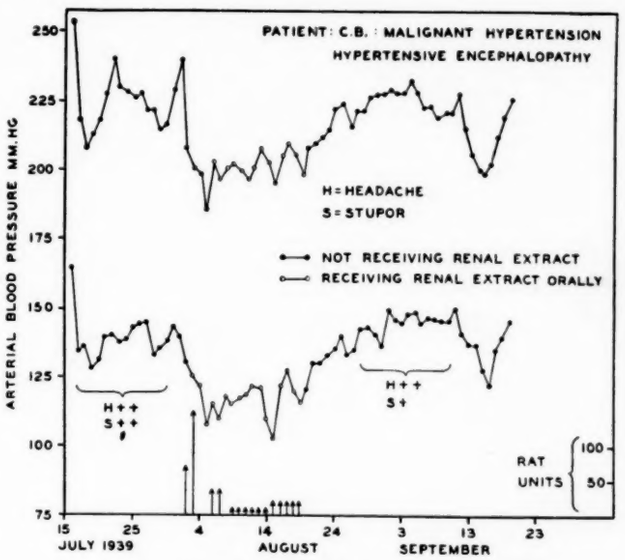


Chart 7.—Although this patient received moderate sized doses of renal extract by mouth over a period of two weeks, no significant decline in blood pressure occurred.

state. After treatment had been discontinued for a number of days the blood pressure gradually rose to approximately the pretreatment level. At the same time the symptoms returned. Two weeks later, however, the patient exhibited spontaneous improvement in symptoms and a spontaneous decline in blood pressure which was less marked and of shorter duration than the decline which occurred during and immediately after the administration of renal extract.

Results similar to those here reported have been obtained in several other patients. These will be reported in detail at a later date. Although all of the patients who have been cited were studied while in the



NOTE: EACH POINT REPRESENTS THE AVERAGE OF 6 MEASUREMENTS TAKEN AT INTERVALS OF 4 HOURS

Chart 8.—This patient was given large doses of the extract by mouth for a period of two days, followed by small doses for ten days. During this period there was a moderate decline in blood pressure and well marked clinical improvement. After the extract had been discontinued the blood pressure rose slowly over a period of ten days to the previous level. At a later date he showed a spontaneous decline in blood pressure, which was less striking and of shorter duration than that which occurred while he was receiving the extract. Symptomatic improvement was marked in this man during the time the extract was being given.

hospital and although with the exception of the first patient the blood pressure had been observed for a considerable time before the administration of renal extract, we prefer to draw no conclusions as regards the therapeutic effect in patients. The subjective improvement which seemed to occur might conceivably have been the effect of suggestion. Although the method of study makes it very unlikely that the declines in pressure could have been spontaneous, this possibility has not been entirely excluded. Extremely large amounts of kidney are required at the present time in order to produce a single human dose. Furthermore, there is at present no certain method of determining which patients have hypertension of renal origin, and it is only on such patients that the extract would be expected to be effective. Finally, since a marked decline in blood pressure occurring after the administration of the extract in animals has frequently been associated with severe untoward symptoms, great caution must necessarily be used in the treatment of patients until more is known of the nature of this reaction. Every effort is being made to overcome these difficulties as rapidly as possible. The fact that Page, Helmer, Kohlstaedt, Fouts, Kempf and Corcoran [23] have subsequently but independently obtained both in animals and in patients results comparable to those here recorded, which confirm our earlier reported work,[24]

23. Page, Irvine; Helmer, O. M.; Kohlstaedt, K. G.; Fouts, P. J.; Kempf, G. F., and Corcoran, A. C.: Personal communication to the authors.

24. Our results demonstrating decline in blood pressure in hypertensive animals and patients following the administration of renal extract were reported before the American Society for Clinical Investigation, May 1, 1939; before the Cleveland Academy of Medicine, September 15; before the Johns Hopkins Medical Society, November 13; before the Washington Heart Association, November 15, and before the American Association for the Advancement of Science, December 29.

strengthens the probability that the declines in blood pressure exhibited by our patients have been due to the therapy rather than coincidental. However, until the difficulties mentioned can be overcome and until a much larger series of patients can be studied, we prefer to regard the studies on patients as inconclusive and as still in the experimental stage.

The chemical nature of the active principle of our extract is still uncertain. Under proper conditions of temperature, salt concentration and p_H the active principle is soluble in 40 per cent acetone and can be precipitated by the addition of further acetone in sufficient quantity. It can also be precipitated by the use of ammonium sulfate or by saturation with sodium chloride. Details concerning the method of preparation of the crude extract have been published elsewhere.[25]

Comparison of Some Properties of the Renal Antipressor Substance with Those of Certain Depressor Substances

Substance	Source	Hypotensive Effect on Experimental Animals: Normal Animals: Decline	Normal Animals: Duration	Hypertensive Animals: Decline	Hypertensive Animals: Duration	Oral Effectiveness Demonstrated	Precipitation by Ammonium Sulfate	Dialyzability	Comment
Histamine	Nearly all tissues	+	Seconds or minutes	+	Seconds or minutes	0	0	+	No depressor effect in etherized rabbits
Acetylcholine	Many tissues	+	Seconds or minutes	+	Seconds or minutes	0	0	+	Depressor effect abolished by atropine
Adenosine (and related compounds)	Muscle, blood (all tissues)	+	Seconds or minutes	+	Seconds or minutes	0	0	+	Causes heart block in guinea pigs
Urohypotensin (Abelous and Bardier)	Urine	+	Minutes	?	?	0	+	0	Constriction of pupil of rabbit's eyes (?)
Kallikrein (padutin) (Frey and Kraut)	Urine, pancreas	+	Seconds	?	?	0	+	0	Inactivated by blood
Depressan (detonin) (Wollheim and Lange)	Urine, posterior lobe of hypophysis	+	Minutes or hours	?	?	0	+	0	Absent from urine in essential hypertension; present in renal hypertension and in normal subjects
McDonald's depressor substance	Liver	+	Minutes or hours	?	?	0	?	?	Precipitated by phosphotungstic acid
Lange's depressor substance	Intestine, mesentery, nearly all tissues	+	Seconds or minutes	?	?	0	+	+	A guanidine derivative ?
Depressor substance of Major and Weber	Brain	+	Minutes	?	?	0	?	?	Not precipitated by silver or by phosphotungstic acid
Substance of Euler and Gaddum	Intestine, brain	+	Seconds	?	?	0	0	+	Contraction of rabbit's intestine
Gomez's depressor substance	Renal cortex	?	?	?	?	0	?	?	Chemical properties and animal experiments not reported
Tubulin (Jablons)	Kidney	?	?	?	?	0	?	?	Animal experiments not reported
Renal antipressor substance *	Kidney	0	0	+	Days	+	+	0	Precipitated by picric acid

* Pharmacologic properties as given refer to effects obtained by oral administration.

RELATION OF RENAL ANTIPRESSOR SUBSTANCE TO OTHER PREVIOUSLY DESCRIBED TISSUE EXTRACTIVES

The renal antipressor substance described in this paper differs in many respects from the depressor preparations reported by others. The table presents a summary of certain simple chemical and pharmacologic properties of the extract as compared with certain nonspecific depressor substances of known chemical composition and as compared with extracts described by previous investigators. The chemical properties and the type of action are entirely different from those of histamine, choline and the adenosine group of compounds. There likewise appear to be distinct differences from the products obtained by others from kidney, and although our extract has certain properties resembling those of urohypotensin and depressan it differs from these in that oral doses which cause marked decline in the blood pressure of animals with renal hypertension have little or no effect on the blood pressure of normal animals. So far as we know, no other substance has been described which has the properties of long duration of action, effectiveness by mouth and lack of reduction of blood pressure in normal animals as compared to marked reduction of blood pressure in animals with renal hypertension. As far as we can judge from the available data, the extracts derived by other investigators from tissues other than kidney display few properties in common with our preparation. More comprehensive investigations concerning the chemical and biologic properties of the active substance are in progress and will be reported on at a later date.

SUMMARY

1. Recent experimental studies indicate clearly that a rational and logical basis exists for the possible therapeutic value of renal extract in hypertension of renal origin.

2. Extracts of the kidney have been prepared which, when administered orally to normal animals, do not produce a decline in blood pressure but have the property of partially inhibiting the pressor effect of subsequently injected renin.

3. When extracts containing the renal antipressor substance in sufficient amount are administered, either parenterally or orally, to animals with experimental renal hypertension, a well marked and prolonged decline in the blood pressure occurs.

4. A small number of patients have been treated by means of the oral or parenteral administration of the renal antipressor substance. In most of the subjects a decline in the blood pressure has occurred. However, for reasons which have been mentioned we prefer not to draw any conclusions at the present time from these observations.

5. The available evidence indicates that the renal antipressor substance has certain unique properties which differentiate it from various depressor tissue extractives described by previous investigators.

710 North Washington Street.

25. Grollman, Arthur; Williams, J. R., Jr., and Harrison, T. R.: J. Biol. Chem. **134**: 115 (June) 1940.

ABSTRACT OF DISCUSSION

DR. MURRAY STEELE, New York: Dr. Harrison has been largely instrumental in bringing before us in this country the work of Tigerstedt and Bergman, which was confirmed and extended by Bigel and Strauss and by Hessel and Hartwich. Shortly after he had become interested in the pressor substances, observations of the behavior of reactions of animals led him to the deduction that there was an antipressor substance also in the renal tissue. From this point on he was fortunate in being associated with Dr. Grollman, and they have this morning presented the results of that work. I should like to point out a phenomenon which is of extraordinary interest in the development of these researches. When interest in a subject is great, many laboratories soon become involved. Since we can in these days disseminate news more rapidly by publication and at meetings, the frequency of simultaneous work and simultaneous discoveries increases and I think this work is an example of that fact. By entirely different reasoning, in two separate laboratories, the same conclusion has been reached at almost the same time. Dr. Harrison, from intimate knowledge of the behavior of animals injected with renin and from the knowledge that removal of the kidneys will increase the rise in pressure obtained with renin, deduced that there was an antipressor substance in the kidney. Dr. Page, in his laboratory, from more purely chemical reasoning, from the fact that in a perfused animal something in the blood was used up which was not the renin activator, yet which prevented the action of the renin-renin activator system, came to the conclusion that a renal antipressor substance developed. Dr. Harrison has emphasized the fact that this depressor substance is costly, very difficult to obtain at the moment, and that it is not yet clear what the clinical uses are or will be. What is clear is that a most extraordinary tool for the further study of the mechanism of the development of renal humoral hypertension has been found.

DR. M. C. WINTERNITZ, New Haven, Conn.: The procedures that have been utilized are valuable in association with humoral pressor effects elicited through the kidney. As a pathologist, my interest lies in structural variants of disease and not in physiologic or chemical detail. During the past year these approaches have been found indispensable. The authors have said everything I might have contributed in discussion and they have been conservative. They have raised the question whether it is desirable to lower blood pressure in renal hypertension. Now that we know hyperpyrexia is of therapeutic value in some diseases and no longer always want to reduce fever, perhaps a similar point of view may be desirable for hypertension. "Renin" is a crude product; its fractions have not been isolated and consequently their chemical and physiologic properties are not known. The ammonium sulfate preparation which the authors mentioned contains pressor and depressor substances as well as agents that necrotize muscle, including heart muscle and the smooth muscle of arteries, veins and other hollow muscular viscera, also diaphragmatic muscle but not skeletal muscle. It probably contains still other factors that result in hemorrhages. The fate of individual substances of such a group when given by mouth is in itself a problem. A similar preparation injected intravenously into dogs with or without kidneys results in vascular lesions of the type that characterize malignant nephrosclerosis. Renin D, I think our chairman has prepared. It has been purified by Dr. Swingle, and my associate Dr. Mylon has carried the separation further. Renin D contains three ferments for which it has been tested and perhaps many more. The three are a tryptic, a peptic and a catalytic type. It also has a high protein content and its nonprotein nitrogen will increase rapidly at body temperature. The enzyme activity and almost all if not all of the protein of renin D are removable. At this stage, when the nitrogen is reduced to 1 microgram for every kilogram of the dog's weight, intravenous injection results in a typical renin elevation of the blood pressure of from 50 to 75 mm. of mercury. Even this product can be shown to be impure by bio-assay. Obviously intravenous use of renin is fraught with danger. Experimentally it has great value for the production of malignant nephrosclerosis with lesions in many important viscera including the myocardium, brain, kidneys and blood vessels. There is no doubt great difference between its administration by mouth and intravenously. Nothing that I have said, therefore, could apply to its use by the first method.

DR. EDGAR ALLEN, Rochester, Minn.: The work which Dr. Harrison and his associates and others are doing is of great interest to those who practice clinical medicine. Many patients with so-called essential hypertension or hypertension of other origins are seen and physicians are desperate for some remedy to take care of these patients. In present day American life essential hypertension seems to be the most serious disease, accounting for at least twice as many deaths as cancer. It would not be fair to leave this discussion on the note that it is not desirable to lower blood pressure in essential hypertension. I am sure that what Dr. Harrison meant to discuss and what Dr. Winternitz wished to emphasize was that it may not be desirable to reduce blood pressure by means of the extract which Dr. Harrison has discussed. However, it is highly desirable to lower the blood pressure of patients with essential hypertension, and when this is accomplished all the serious effects of hypertension disappear. The work which began with Dr. Goldblatt and has been carried on by Dr. Harrison and his associates and others has been of great interest to experimental medicine. It does not detract from this work to say that with minor exceptions it has not been of any help to clinicians who take care of patients with essential hypertension. The single exception to date is that occasionally one sees a patient with hypertension which is indistinguishable from the so-called essential hypertension in man, which is renal in origin and which has been cured by the removal of a diseased kidney. There are in the literature at least 100 remedies for essential hypertension, and the conservative way in which Dr. Harrison has approached this problem precludes the possibility that there would be unjust claims by him or his associates. However, if the usual program follows, there will be unjustified claims by others. The implication has been that, since this extract reduces the blood pressure of animals with experimental hypertension and does not reduce the blood pressure of animals with normal blood pressure, it has a specific effect on the genesis of hypertension induced experimentally. However, it is easy to reduce the blood pressure of many patients with essential hypertension and quite difficult to reduce the blood pressure of patients with normal pressure. Sleep may reduce the blood pressure of a patient with hypertension from, say, 240 systolic to 160 systolic, or 140 systolic, but sleep will not reduce the blood pressure of a patient with normal blood pressure more than 10 or 15 mm. of mercury. It would not be fair to conclude from this observation that the reason the patient with essential hypertension has elevated blood pressure is that he has not had sleep. It is true only that it is easier to reduce the blood pressure when it is elevated than when it is normal.

DR. FREDERICK M. ALLEN, New York: The problem of renal-vascular disease is so complex that a coordinated approach is apt to be most productive, as I believe was illustrated by our investigation which began in Morristown in 1920, following the same lines as had previously been pursued in diabetes. For historical interest, and in behalf of about a dozen former co-workers, I wish to mention the following published results: 1. Extensive studies with partial nephrectomy furnished the first demonstration that the principal phenomena of nephritis are explainable by simple quantitative reduction of functioning renal tissue. 2. Explantation of the kidneys was devised for various investigative purposes, which could only partly be carired out. 3. With the aid of a new auscultatory device for routine pressure readings in dogs, the first discovery of experimental chronic hypertension was made by clamping the kidney blood vessels, a method which not only holds priority but which also can be shown to be still the best hypertensive method for some purposes. 4. Therapeutically, rigid exclusion of salt from the diet was proposed. Here disputes can confidently be left to ultimate decision on one single unavoidable issue, namely accuracy of clinical observation. 5. No study was made of Tigerstedt's hypertensive substance renin, but an attempt in the direction of organotherapy yielded the first discovery of an acid-alcohol extract of fresh kidneys which was able to reduce blood pressure. In view of the recent activities along all five of these lines, it is worth noticing that all these developments would have been equally possible fifteen years ago. The delay has been

due solely to the power of a monopolistic autocracy not only in controlling but in suppressing research. There were also other fundamental lines of investigation, besides the five mentioned, which were not published and have not been discovered elsewhere; and no lack of effort on my part has been responsible for stopping both this and my diabetic work. The kidney extract research would have been lost altogether if it had not been continued by Dr. Jablons. He seems to have a priority of several years in some methods of purifying the extract and in studies of sodium and potassium, which may explain some of the variable or fatal results described by others. I have not been able to keep in touch with details of the recent developments in this field, which are both brilliant and confusing. Dr. Harrison and his collaborators are to be congratulated on their reported success with oral administration, and the papers by other authors have combined to make this one of the subjects of leading interest in this convention. Nevertheless, I revert to my original statement concerning the complex renal-vascular problem. Kidney extract does not furnish the entire solution of this problem. However great its theoretical or practical importance may prove to be, I think most investigators will join in warning practitioners that no spectacular remedy like insulin is at hand. We may be on the way, but we have not yet reached any certainty regarding either the cause or the cure of essential hypertension.

DR. BENJAMIN JABLONS, New York: Dr. Harrison's report is heartening to those of us who have been active in this field for some time. I have been working with kidney extracts for nine years. During that time two outstanding facts have become apparent, and the work of Dr. Harrison, Dr. Page and others confirms them. The first is that the hypotensive extract is not easily obtained. While a laboratory extract will give very startling results used on patients or in experimentally induced hypertensive animals, the same material produced on a large scale in a pharmaceutic plant will often not give the same results. The second is that suitable cases must be selected. In analyzing failures I have found that it was important to make certain that the individual for whom this extract is to be used does not have irreversible changes in the arterioles. Recently I have tested a number of these cases for the presence of peripheral vasospasm and have found it in a considerable number of cases of essential hypertension. If kidney extract produces peripheral vasodilatation, one is encouraged to proceed with its use and can expect satisfactory results. Another reason which I believe contributed to failure in some instances was the presence of protein in the extract. For eight years I have been working with a protein-free extract. With this protein-free, aqueous acid-alcohol extract I have obtained some very startling results. I have also had a number of failures. We are indebted to Dr. Harrison and his co-workers for emphasizing the oral use of extract. A few years ago I used it orally without results. Encouraged by his published results, I have again used our extract orally in seven cases. Four responded, two failed, and in one case the condition was definitely aggravated. Our extract is not toxic to animals in doses below 6 per cent of body weight. It is prepared by a method presented before the New York State Medical Society in May 1937 and published in the Jan. 1, 1938, issue of the *New York State Journal of Medicine*. One case of malignant hypertension has been under treatment since May 1933, and many others of shorter duration have shown no toxic effects. By watching the blood electrolyte concentration and chloride excretion in the urine, one can determine indications and contraindications for extract administration. The summarized results will be published shortly.

DR. T. R. HARRISON, Nashville Tenn.: I agree with Dr. Winternitz that an ammonium sulfate precipitate has in it many things, and it is because of this fact that we have mainly employed oral administration even though larger amounts are needed. We are hoping that the time will soon come when we may be able to purify the material better and shift over to parenteral therapy. As to whether it is desirable to lower the blood pressure, I think it is but am not certain. The question is, Is it desirable to lower it to normal, assuming one could? That I don't know, and certainly some of our animals have died when the pressure has been lowered to normal. We aren't certain that the lowering of blood pressure has been the cause of death. It may have been due to some impurities in the extract. But until we get over that hurdle we have to be extremely cautious. About the specificity, our own evidence suggests that the material is specific for kidney but more studies are necessary before we can be certain. The difficult question as to whether essential hypertension is renal I am going to dodge by saying that in my own opinion, which is subject to revision at any moment, some instances are and some are not. I should like to point out to Dr. Jablons that there have been no deaths of patients in Nashville, and Dr. Page tells me none in Indianapolis. Because of the deaths of animals one has been cautious about administering this to human beings. I think that if some of the previous workers had studied hypertensive animals before they studied hypertensive patients their problems might have progressed more rapidly. This isn't confirmation of Dr. Jablons' work. Dr. Jablons reported that with a fraction obtained by extraction of kidney in about 95 per cent acid alcohol he could obtain an active blood pressure lowering substance. One of the methods we frequently use to make our material is to collect it in 95 per cent acid alcohol, but we throw away the material that is soluble in 95 per cent acid alcohol, which is what Dr. Jablons uses; and the material that is insoluble, which Dr. Jablons discards, gives us the typical results, so that it is quite clear that Dr. Jablons is dealing with one kidney extract and we are dealing with another, and that they are not the same thing. Which is the better kidney extract, time will have to tell.

OSTEOMYELITIS OF THE SKULL FOLLOWING FRONTAL SINUSITIS

A. S. MACMILLAN, M.D.

BOSTON

Before considering osteomyelitis as a complication of frontal sinusitis it might be well for me to review briefly the roentgenologic aspects of the acute and chronic infections in this area which have traveled up the frontonasal duct.

Before one can arrive at an intelligent interpretation of the density of a sinus as seen in the postero-anterior view, one must examine the lateral view for the depth of the sinus and for the thickness of the anterior and posterior walls and note any irregularities in both depth and thickness. One must then note the character of the bones of the skull—the relative thickness of the cortex to that of the medulla. Then, and only then, can the density one expects to find in the frontal view be evaluated.

The minimum number of views that should be taken are four, namely a lateral, a postero-anterior, a Waters position in the prone and a fluid level position.

When the nasofrontal duct becomes completely or partially blocked, the membrane thickened and its secretion retained within the sinus, it is always surprising how little increase there is in density over the normal. Often the difference in density between the two frontal sinuses is so slight, even when they are completely filled, that other means of diagnosis must be looked for. In this connection it must be remembered that normally there may be an opening in the bony septum between the two frontals, and when this occurs the membrane of the normal sinus becomes thickened and pushed away from the interfrontal septum.

It is a well established fact that acute inflammation of the mucous membrane causes decalcification of the underlying bone. This is as true in acute frontal sinusitis as it is in mastoiditis. One change I look for in mastoiditis is decalcification of the mastoid cell

Read before the joint meeting of the Section on Laryngology, Otology and Rhinology and the Section on Radiology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

partitions. I expect this to occur in from seven to ten days after onset of infection of the mucous membrane. In frontal sinusitis one must watch for this decalcification. Loss of the entire outline of the sinus due to this loss of the inner cortical lining is to be

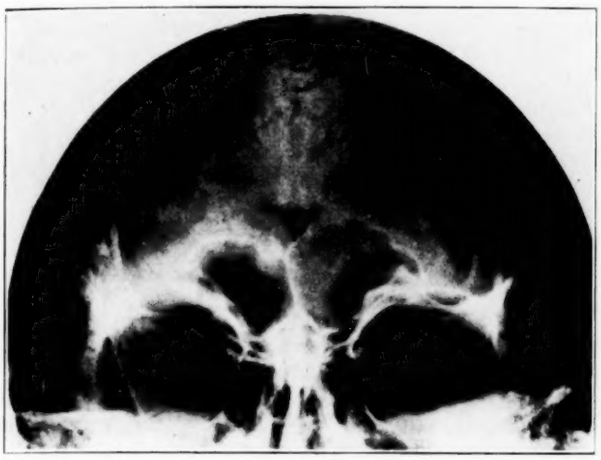


Fig. 1.—A white youth aged 16 had a history of sinusitis with swelling about the left eye three weeks before admission. This subsided. Two days before admission swelling of the left eyelids recurred and there was swelling about 2 cm. in diameter in the midline above the frontal sinus. A roentgenogram revealed an area of osteomyelitis at this point. Removal of a wide area of bone including the necrotic area resulted in recovery without complications.

expected, but localized loss of the outline is an entirely different matter.

In subacute and chronic sinusitis, lasting a matter of weeks, there is an increase in density of the anterior and posterior walls and the surrounding bone, nature's walling off process. This eventually results in sclerosis so consistently seen in these chronic infections. At

Fig. 2.—A white girl aged 16 years had a history of infection of the upper respiratory tract and frontal headache fifteen days before admission. Four days later she had swelling and edema of the forehead—development of an orbital abscess—which was drained with complete subsidence of all symptoms. Nine days later severe frontal headache, nausea and vomiting occurred. Examination revealed evidence of a brain abscess of the left frontal lobe. This was drained. The sinuses at this time were perfectly clear. One month later, with no intervening symptoms, edema and tenderness developed over the left eye. X-ray examination disclosed osteomyelitis of the front wall of the frontal sinus extending out into the frontal bone; radical removal of the bone was done and recovery was uneventful.

times it is difficult to make out fluid levels through this sclerosis, again showing how small a part the density of the contents of the sinus has to do with the total density.

The progress of infection of an acute frontal sinus, which must be watched for, is the change in density, loss of its outline and the reaction in the surrounding bone. In a case of severe acute infection in which frontal headache is accompanied by swelling and edema of the tissues over the outline of the sinus, but sharply limited to the area of the infected sinus, a constant watch should be maintained for minute perforations of the anterior wall. These perforations are caused by the enlargement of the thrombosed small penetrating vessels coming through the bone from the infected mucous membrane. These minute perforations can be detected in the anterior views and are one of the early x-ray signs of bone infection. Localized loss of the outline due to actual necrosis of the wall at one point is an important accompanying finding. A tangential view of the frontal wall in question may show localized necrosis. Infection must be present at least a week before these signs become evident.

Involvement of the posterior wall of the frontal sinus may be determined by noting the change in the

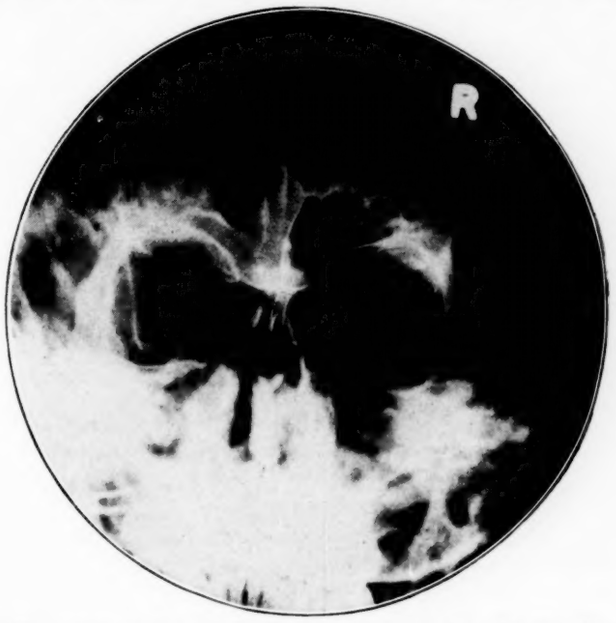


Fig. 3.—A white man aged 25 had left pansinusitis with an orbital abscess. An external frontal operation (Lynch) was done; ten days later there were signs of an intracranial pathologic condition. He was referred to the Massachusetts Eye and Ear Infirmary. Examination revealed osteomyelitis extending by thrombophlebitis from the outer border of the left frontal sinus. At operation a large extradural abscess was found. Recovery resulted.

pattern of the composite picture of the anterior and posterior walls, as seen in another view. If the infection remained in the mucous membrane, or even in the bone, conditions would not be so serious.

The thrombosed vessels of the mucous membrane which carry infection into the bone are continuous with those entering the dura and brain, and blood sinuses, and may produce infection in these areas. These serious complications may occur simultaneous with the bone infection so that an apparently solid posterior wall of an infected frontal sinus may be covering an extradural or brain abscess.

The frontal bone is rich in diploetic veins. Two fairly constant plexuses occur at the outer angles in the region of the frontal bossae. Others may be seen to course through the walls of the frontal bone and enter blood lakes or parasinoidal sinuses, which in turn empty into the longitudinal sinus. For the many veins large enough to be seen on the x-ray films there are

also many microscopic ones that are as important in the process of dissemination of the infection. These blood vessels and sinuses should be watched for either any change in their outline or any loss of density in the surrounding bone. This involvement in the diploe is

Fig. 4.—A Negro aged 19 years had left frontal sinusitis with extension of infection into the left frontal bone; operation consisted of removal of the infected bone and some normal bone, working from the infected area outward. This conservative operation was followed by further extension and the development of a brain abscess from which the patient died. Osteomyelitis of the skull cannot be dealt with in a conservative manner.

very rapid, and change can be detected from day to day on the x-ray film.

My experience with the x-ray appearances in infection of the frontal bone, secondary to frontal sinusitis, extends over a period of twenty years, during which time I have seen a marked change in treatment of osteomyelitis. In the eighty-six cases which I have seen at the Massachusetts Eye and Ear Infirmary, the infection was limited to the front or posterior wall of the sinus. The mortality in the group was 14 per cent, deaths being due to epidural abscess, subdural abscess, brain abscess or meningitis. Thirty-six patients developed osteomyelitis extending beyond the limits of the frontal sinus into the frontal bone (figs. 1, 2 and 3).

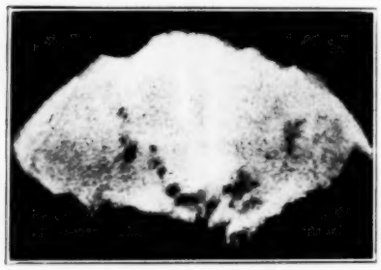


Fig. 5.—Reproduction of a roentgenogram of a removed fragment of frontal bone measuring 10 by 5 cm., showing in the lower part the outline of the frontal sinuses and above the osteomyelitis breaking out along the thrombosed diploetic veins. Microscopic examination of the decalcified bone showed marked involvement in the areas that appeared normal by x-ray examination.

Spreading osteomyelitis is a disease affecting the young. Of our thirty-six patients, half were in the second decade of life and eleven in the third decade. Staphylococcus aureus was the usual infecting organism.

It is in the treatment of this group that a great change has taken place. In the earlier days the surgeon usually waited for x-ray signs of osteomyelitis. When the diagnosis was made by the roentgenologist, the necrotic bone and some of the normal bone were removed. It was not fully realized that the bone would be infected for from 1¾ to 2 inches beyond the necrotic area discernible on the x-ray film. If the surgeon wished to be conservative he waited, hoping that the lesion would localize and that sequestrums would form which he could remove. The tragedy of this method was that in every case in which sequestration was awaited a fatal complication arose.

During the time when the delayed or incomplete type of operation was in use frequent x-ray examinations were made to see whether any further involvement was taking place. The mortality rate with this type of puttering surgery was high, 58 per cent (fig. 4).

In the last seventeen cases a large part of the frontal bone was removed in one operation, including the infected area, and out into healthy bone for upward of 2 inches, thus eliminating osteomyelitis, the cause of the complications (figs. 5 and 6).

In the fulminating cases operation was done before any indication of involvement could be seen by x-ray examinations for the diagnosis depended entirely on the one all important sign of pitting edema. Microscopically the removed bone has always been found to

Fig. 6.—Appearance eighteen months after radical removal of part of the frontal bone for extensive osteomyelitis. This also shows the first bone graft put in by the plastic surgeon to cover the defect.

be thrombosed with infected veins; in a number of these cases x-ray examination of the specimen showed nothing to suggest the diagnosis. This form of treatment has reduced the mortality to 25 per cent, and if the two cases in which operation was done in the presence of an overwhelming fulminating meningitis are eliminated from this count, the mortality would be down to 12.5 per cent. The meningitis in these cases arose from an infection of the upper respiratory tract of from four to five days' duration. There was pus in the frontal sinus and pus oozing from the cut surface of the bone even at the hair line. In such cases the operation could be regarded only as a gesture.

CONCLUSION

1. Osteomyelitis of the skull, because of its complications, is a most serious disease.

2. The x-ray evidence of this disease should not be waited for in the presence of clinical evidence.

3. Pitting edema to the hair line is a positive sign of infected bone.

4. Puttering surgery invites disaster.

483 Beacon Street.

OSTEOMYELITIS OF THE FRONTAL BONE

AS A COMPLICATION OF FRONTAL SINUSITIS

H. P. MOSHER, M.D.

BOSTON

Osteomyelitis of the frontal bone is one of the most dreaded of surgical diseases and one of the most fatal. In some parts of the country osteomyelitis of the frontal bone as a complication of infection of the frontal sinus is a rare disease. In my locality the fulminating type, and most of our cases fall into this class, is fairly common. Osteomyelitis of the long bones of the leg occurs over wider areas. When a disease is deadly, when patients suffering from it may come first to the general practitioner, the surgeon or the specialist and when recent work has been done on the disease the results of which are not yet in the textbooks, I feel that it becomes a subject of general interest. At least this is my hope. Also this is my alibi for presenting the subject today.

During the past seven years I have begun to approach these cases with more confidence. This is due to what I have learned by the systematic microscopic examination of specimens of osteomyelitic bone removed at operation during this period and by routine interval roentgenograms before and after operation. This continued study has made the source of the infection, its manner of spread and the speed of the spread clearer. This knowledge has led to the adoption by us in the fulminating type of a radical early operation which meets the disease head on instead of by the customary prolonged and generally unsuccessful pursuit from the rear. The infection in these cases does not wait while the surgeon watches and waits. It must be dealt with by an early "blitzkrieg."

So much by way of introduction. In former papers I have dealt with the subject of osteomyelitis of the frontal bone somewhat exhaustively. The space allotted for this paper permits only a condensed review.

THE ORGANISM

The organism in osteomyelitis of the frontal bone generally is Staphylococcus albus or aureus, and occasionally the streptococcus.

THE TYPES OF OSTEOMYELITIS

The disease occurs as two types—the fulminating, rapidly spreading form of which swimming is a frequent cause, and the less virulent localizing form which tends to burn itself out and form sequestrums. If the patient is septic, with pitting edema of the skin of the forehead half way to the hair line or at the hair line as often happens, I consider this as the fulminating type. Not having second sight; I cannot pick the case in which it is safe to operate conservatively and do what might be called a minor operation and hope for sequestration. I am not slipping into the grand manner when I say that on the time and the type of operation which the surgeon elects hangs the life of the patient.

THE DIPLOETIC VEINS

The diploetic veins of the skull are numerous and connect superficially with the veins of the scalp and have deep connections with all the blood sinuses of the skull. The diploetic veins of the frontal bone are a continuation of the veins of the mucous membrane of the frontal sinus. Relatively they are very large and are absent from the frontal bone in only 3 per cent of the cases. The infection in the frontal sinus produces thrombophlebitis of the veins of the mucous membrane and of the diploetic veins of the frontal bone. The infection spreads to the bone marrow in which the veins are located. The branches of the diploetic veins run outward to the periosteum of the frontal bone and inward to the dura. The dura seems to attract the infection more strongly than the periosteum.

As everything in osteomyelitis of the frontal bone complicating frontal sinusitis harks back to infection of the mucous membrane of the frontal sinus and its walls, I shall have to bore the reader with the changes which infection causes in these structures. In no other part of the body do the pathologic changes caused by infection determine so definitely the course of the infection, its manner of spread and, most important of all, the type of surgery to be employed if it is to be successful and the time when this surgery is indicated.

THE BONE MARROW

There are two kinds of bone marrow—the yellow or fat marrow and the red or blood forming marrow.

Yellow marrow looks like a collection of fat cells. Between the fat cells there are narrow stellate spaces which are potential blood lakes. The cells lining the stellate spaces are capable of great activity in the production of fibrous tissue.

The red bone marrow, instead of having the empty look of the fat marrow, is crowded with every type of blood cell and every ancestor, immediate and remote, of the various types of blood cells. It is a bewildering maze not as yet fully deciphered. It still offers a fertile field for dispute among the experts. The diploetic veins run in both fat and red marrow.

THE CHANGES PRODUCED IN BONE MARROW BY INFECTION

The changes which infection produces in bone marrow occur in a definite order. The veins in the fat marrow enlarge greatly and often break, causing hemorrhage in the marrow space. Very early, so early that it almost seems to occur at the same time, the veins enlarge and a protective fibrosis begins in both the yellow and the red marrow. If the infection wins out over the protective fibrosis, patches of bone die and form sequestrums. In the neighborhood of a sequestrum the osteoblasts work hard to form new bone. As an added means of protection in nature's fight to conquer the infection, a layer of new bone made up of very fine trabeculae is often laid down over the dura. This, however, is so often found to be infected that it seems to be more of a carrier of infection than a barrier to its spread.

The only thing in this picture that is not familiar is the early protective fibrosis which forms in the marrow cells. On seeing it, one feels that nature is doing its best for the patient from the very beginning.

SIGNS AND SYMPTOMS

As osteomyelitis of the frontal bone is in most cases a complication of acute infection of the frontal sinus, there are classic signs and symptoms which go with this condition. Pitting edema of the skin of the forehead (Pott's puffy tumor) is the first sign of involvement of the frontal bone. Microscopic examinations of bone

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specimens have shown that the limit of the edema is a practical guide, and the only guide in fact, to the limit of infection in the bone marrow. In fulminating cases the edema quickly extends to the hair line. The patient's temperature rises according to the amount of toxins absorbed from the infected veins and marrow spaces. X-ray examination shows a cloudy frontal sinus and gives the number and position of the diploetic veins. As it takes from seven to ten days for bone necrosis to occur, the x-ray film is not positive for osteomyelitis until this time has elapsed.

When the edema is localized and does not extend, as happens in the rare case in which trauma is the cause of the osteomyelitis, the infection of the bone marrow may also be localized.

The microscopic examination of osteomyelitic bone specimens has given another practical point, namely around an area of necrosis the infection extends radially for from 1½ to 2 inches. The applied value of this finding is evident.

COMPLICATIONS

Few surgical infections have more possible and immediate complications. Unlike osteomyelitis of the long bones, which is often tempestuous enough, osteomyelitis of the frontal bone has the dura and the brain as neighbors. This means that extradural and subdural abscess, meningitis and brain abscess are common complications and are always in the offing. In osteomyelitis of the tibia the infection runs along under the periosteum as it does in infection of the frontal bone and the marrow also is infected, but the tibia has not the bad acting neighbors which the frontal bone has. The old saying about a lighted match near a powder keg aptly applies to osteomyelitis of the frontal bone, only there are two powder kegs to blow up instead of one.

SURGICAL TREATMENT

When edema of the skin of the forehead extends to the hair line, as it quickly does in fulminating cases, I believe that the surgical treatment of choice is the removal of practically the whole of the frontal bone. I should do this even if the edema extended only half way to the hair line. Laterally removal of the bone should extend to the external angular process of the frontal bone on both sides. It is neater craftsmanship to remove the bone in one piece.

THE CUTANEOUS INCISION

The median T incision gives the best exposure and the best drainage. The stem of the T should begin at the hair line.

The arms of the T should be made at the upper limits of the eyebrows, not through them. A split eyebrow comes together poorly when the operation for the correction of the operative deformity is done. The area of bone to be removed is marked out with the electric burr and the burr holes are connected by means of the Gigli saw or rongeur. Usually the bone dissects easily from the superior longitudinal sinus. The greater part of both the front and the posterior wall of both frontal sinuses is removed in order to let the sinus obliterate. This I believe is the surest way to obliterate the frontal sinus, even in nonosteomyelitic cases.

The triangular skin flaps are sutured to the scalp and the wound is left wide open. The dura is protected with paraffin gauze. For most operators fancy and fashion have determined the solutions used on the dressings if anything other than salt solution is employed. One by one bactericidal vaccines have appeared and have been used with much trumpeting, only to disappear from the literature in a short time.

I hold that it should be routine practice to open both frontal sinuses and remove the anterior and posterior walls of each. Both sinuses are usually infected or well on their way to infection. In order for one to be sure of what is going on both sinuses have to be opened. The x-ray film is an unreliable guide on this point.

When the bone to be removed has been marked out with the burr, it is not uncommon for the patient's condition to become poor. The operation is thereupon stopped and the patient given a transfusion on the table, to be repeated if necessary when he reaches his bed. This means that donors should have been selected to be available at once.

THE TIME OF CLOSURE OF THE OPERATIVE WOUND

From my experience I feel that three months is as early as closure should be attempted. Secondary operations in a number of cases have been necessary when a shorter period was tried. During the waiting period for the performance of the plastic repair the edges of the bone defect are watched by x-ray examination for recurrence of the osteomyelitis. This waiting period is hard for the patient because the preliminary deformity is often marked.

In one of the early cases in which closure was done at six weeks the patient had jacksonian convulsions at irregular intervals for a few months. I am wondering whether, had closure been delayed, the fibrous tissue which replaces granulation as the end result of the healing process would not have been more evenly distributed and not given the localized pressure which caused the convulsions.

THE REPAIR OF THE OPERATIVE DEFORMITY

The operation for osteomyelitis of the frontal bone is easy. The hard thing about it is to make up one's mind when to operate and what type of operation to use. The plastic repair, on the contrary, is the hardest of the surgical procedures called for in dealing with this condition. The repair of the deformity is not a job for the beginner in plastic surgery. Fortunately my associates and I have Dr. Kazanjian, who is anything but a beginner. The first step in the repair is to free the cutaneous flaps and the periosteum and bring the edges of the periosteum together as close as possible and then approximate the cutaneous edges neatly. After a wait of from twelve to eighteen months for bone regeneration in the operative defect, the deformity is corrected by the insertion of a bone implant or implants, as the case may require. At first these were taken from the crest of the tibia; now Dr. Kazanjian takes the implant from the crest of the ilium, because this has the right curve. A large piece is used to make the lower part of the reconstructed brow. Above this a smaller piece is placed. If this does not prove to give sufficient correction, at a later period cartilage or fat is used to supplement the bone. After this series of steps the deformity is corrected fully 90 per cent. The net result of all these operative measures in 80 per cent of the cases is a live patient and a moderate and bearable deformity.

At this point I wish to remind the ophthalmologists that osteomyelitis of the frontal bone has been known to follow orbital abscess. In a few cases the pus in the orbit is not really an orbital abscess but comes from the frontal sinus by means of a break in the floor of

this sinus. In most cases of true orbital abscess the infection originates in the ethmoidal labyrinth and should be dealt with by an external operation on the labyrinth. What might be called the Italian method of treatment, universally practiced up to a few years ago, consisted in repeated stabbing of the orbit above and below the globe of the eye, often boxing the compass a number of times. The usual result was that recovery took from six weeks to six months. At times, however, osteomyelitis of the frontal bone resulted. I know of a recent case of orbital abscess treated in this inadequate fashion which ended up with osteomyelitis of the frontal sinus, then of the frontal bone. This was followed by brain abscess and death. I am confident that the examination of the old hospital records of any eye clinic would uncover a number of such cases.

REPAIR OF THE BONE DEFECT

In our cases nature's repair of the operative defect has been good only in young patients; in adults it has been very slow. Dr. Kazanjian suspects that we have maltreated the periosteum in the first stage of the operation. We were then thinking more of circumventing the infection than of the operative deformity. Now that we are surer of what to expect from operation in these desperate cases, he feels that more care should be given to preserving the periosteum at the first operation and in freeing it and bringing it together in the plastic operation.

Sprinkling bone dust on the dura is an old procedure. It was used successfully during the World War. Skillern uses it in connection with primary closure of the operative wound.

COMMENT

There are several unsolved questions in the management of osteomyelitis of the frontal bone: Is there any place for the conservative operation in osteomyelitis of the frontal bone? Is primary closure ever permissible? Is there any way of telling at the outset of a case whether it is to be of the sequestrating, mild, localizing type or whether it is of the fulminating, rapidly spreading type almost sure to be quickly complicated with extradural or subdural abscess, or brain abscess and, unless halted in its tracks, nearly always fatal? Am I advocating an unnecessary, radical operation in the fulminating type of case?

First under consideration is the question of overoperating in the fulminating case. I have never had any sureness of result in these cases until the radical procedure as here described was adopted. The microscopic appearances in bone specimens speak for this type of operation. I shall wait for operators to get as good results with a more conservative operation before I give it up. In the fulminating cases I do not think primary closure of the wound is good practice.

The virulence of osteomyelitis varies in different parts of the country. This sounds like an alibi. A recent English writer reported seven cases of chronic osteomyelitis and stated that he had never seen a fulminating case. Reports in the literature of localizing osteomyelitis cured by conservative operations appear from time to time. A number of years ago a certain pugnacious gentleman stated that there was sequestration in all his cases. He has recently made equally strong statements on another subject—this time in connection with an operation on the ear. His listeners then and now were not in full agreement with him.

I should be willing to vote an antemortem halo to the man who can pick out at the onset and be right 75 per cent of the time which case will localize and not present complications.

As far as I can go in picking a case which suggests a conservative operation, it would be a case having the following history and one which shows the following signs and symptoms: The patient, child or adult, gives a history of trauma to the forehead. There is a localized area of pitting edema of the forehead, perhaps the size of a quarter (24 mm.), and the edema does not involve the front wall of the frontal sinus. The patient is not acutely ill. X-ray examination shows no involvement of the frontal sinus and there are no diploetic veins running from the edematous area. If the disease is of a week's standing the x-rays will probably show some necrosis of the bone under the edematous area.

Such a case would indicate and justify a conservative operation. Before operation pus might be withdrawn from beneath the periosteum where the swelling occurs, the organism identified and its virulence tested on animals. If the surgeon is right in his guess that the infection is of low virulence, a wait of forty-four hours for the result of the inoculation test would do no harm.

In a case of acute infection of the frontal sinus in which there is edema of the skin over the front wall of the sinus and no edema of the skin of the forehead, there is osteomyelitis confined for the moment to the front and posterior walls of the sinus. Microscopic studies have made it certain that in such cases there is infection of the posterior wall of the sinus as well as of the anterior wall. This means to my mind that after a portion of the front wall has been removed a part of the posterior wall should be removed as a routine. The object of this is to learn the condition of the dura and to determine whether or not an extradural abscess is present. When there is a necrotic area on the posterior wall it has long been the custom of operators to remove it, and many an unsuspected extradural abscess has been found in time to prevent osteomyelitis of the frontal bone or a brain abscess. For the patient's safety it is our duty to find out what is going on behind the posterior wall when edema of the anterior wall shows osteomyelitis of this wall.

In a case of mastoid disease, if the operator does not find enough pathologic change in the mastoid process to satisfy him he uncovers the lateral sinus.

A part of the posterior wall of the mastoid process lies against the lateral sinus; the posterior wall of the frontal sinus lies against the dura. One can tell the condition of the lateral sinus only by uncovering it. The same applies to the dura as it lies behind the posterior wall of the frontal sinus.

There are not a few men handling surgical cases who are not temperamentally surgeons. They do not think surgically. They are among those who use a hammer occasionally but never can drive a nail straight.

These sentences are inspired by the entrance of chemotherapy into the picture of osteomyelitis. It may change the picture of the treatment of osteomyelitis markedly. It will require good judgment and full surgical judgment to assign it its final role in this disease.

I have given the picture of osteomyelitis as I see it to date. Tomorrow is in the hands of Fate.

SUMMARY

The veins of the mucous membrane of the frontal sinus are continuous with the diploetic veins of the frontal bone. Compared with the thickness of the frontal

bone, they are of enormous size. In diameter they often measure one third to one half its thickness. The infection originates in the frontal sinus and is carried to the frontal bone by the diploetic veins. The branches of these veins run to the periosteum and cause edema of the periosteum and the skin. They also carry the infection to the dura, and the dura seems to attract the infection even more strongly than the periosteum.

If the infection is halted by a thrombus sufficiently long at any given point, there is necrosis of the bone and the formation of a sequestrum. If the edema extends to the hair line, as it generally does in a fulminating case, the infection in the bone marrow has advanced to the same point. The x-ray examination is positive only after necrosis has begun, and it is not positive until from seven to ten days after the onset of the pitting edema. From the surgical standpoint these are the days of hopeful surgery. If an area of necrosis is shown by x-ray examination or is found at operation, the microscopic examination of numerous specimens of bone in such cases has shown that the bone is actively infected for from 1½ to 2 inches beyond the necrotic area. The progress of the infection along the vein which is chiefly infected can be watched by means of the x-rays.

CONCLUSIONS

The operator who is doing his first operation on osteomyelitis of the skull should expect extradural abscesses as a matter of course. In fact he should expect more than this; he should be on the lookout for a subdural abscess or a brain abscess. The brain abscess, if present, is usually found later, or it comes later as a complication, but it is always threatening and should be watched for even at the first operation.

The more I see of fulminating osteomyelitis of the frontal bone, the more I believe that the whole face of the frontal bone should be removed, from the hair line to the eyebrow, as a routine procedure. Preferably it should be removed in one piece and the operation should start in clean bone; that is, at the hair line. However, if the patient is in poor condition and there is an area of necrosis, it is justifiable to work from the necrotic area outward, the bone being removed from 1 to 1½ inches in all directions from the necrotic area. Further, both frontal sinuses should be opened and the anterior and posterior walls of each sinus removed. I am firmly of the opinion that the lateral limit of the bone flap on each side should be at least the outer angle of each frontal sinus or, better, the outer angular process of the frontal bone on each side. The objection to this extensive removal is the deformity. However, since it has been proved that fully 90 per cent of these deformities can be corrected by modern plastic surgery, the surgeon should not allow his work to be restricted by the question of deformity. If he does, he will lose many or most of his cases of fulminating osteomyelitis of the skull.

The mark of osteomyelitis is written on the patient's brow. Cain, you remember, also had a mark on his brow. In the treatment of his patient let the surgeon beware lest he unwittingly reenact the role of Cain and deserve the same telltale mark when he too, by delayed or inadequate operation, kills his brother. Instalment operating in cases of fulminating osteomyelitis of the frontal bone generally results in the patient being repossessed by his maker.

243 Charles Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. MACMILLAN AND MOSHER

DR. ARTHUR C. JONES, Boise, Idaho: Dr. Mosher's comprehensive paper on osteomyelitis of the frontal bone following sinus infection covered all the histology and pathology that I have been unable to find in any of our modern textbooks. I heartily concur with Dr. Mosher when he says that we must meet the fulminating type of osteomyelitis head-on instead of through the unsuccessful rear approach. I recently reported thirteen cases in the majority of which there was a Staphylococcus albus or aureus infection. I have also encountered the pneumococcus. I have found it necessary to remove the entire frontal bone in all my cases. The diploic spaces are tortuous and the osteomyelitis tends to follow the diploic spaces. I remove the osteomyelitic bone as far as the infection extends and then remove normal bone for at least one-half inch. This less radical procedure makes for less disfigurement and takes much less time. Dr. Mosher speaks of the mark of Cain being written on the patient's brow unless the radical procedure is followed. The follow-up pictures of these cases in which the flaps had been pinned back for two or three months have a mark that will tell the whole world that the unfortunate victim has encountered either a buzz saw or a thoroughgoing surgeon. Unfortunately, few of us have a Kazanjian to mop up after us. I envy Dr. Mosher and his staff the privilege of calling in such an eminent radiologist as Dr. Macmillan. Dr. Macmillan has emphasized the necessity of taking at least four views in these cases. Osteomyelitis is about ten days in advance of the x-ray appearances. When the nasofrontal duct becomes completely or partially blocked, the membrane thickened and its secretion retained within the sinus, it is always surprising how little increase there is in the density over the normal. For the most part I use the coronal incision and have been able to uncover as large an area of bone as in the T type of incision. I have had one death in thirteen cases and can see no reason for the T shaped incision, which causes the marked deformity. Of course, the picture of the plastic repair shown by Dr. Macmillan is very complimentary to Dr. Kazanjian. I have seen other pictures with more disfigurement than the ones shown.

DR. JOSEPH E. J. KING, New York: I agree with Dr. Mosher and Dr. Macmillan. There may be a little difference of opinion regarding a few minor details in the operative procedure. I am glad to hear Dr. Macmillan call attention to making x-ray films at short intervals in cases in which one may suspect development of osteomyelitis following disease of the frontal sinus. I have seen cases in which x-ray examination has been delayed so long that it became necessary to remove an enormous portion of the skull. Dr. Fred Law and I have noticed in reviewing films in reverse that a light area representing the point at which osteomyelitis is developing can be seen on the x-ray films at least ten or twelve days before the typical moth-eaten appearance is observed on the films. It is necessary to make only one postero-anterior film every day or two in order to detect this area a number of days before the subcutaneous pus pocket ("Pott's puffy tumor") makes its appearance. This thinned out area is due to involvement of the bone and is observed usually about three-fourths or 1 inch above the supra-orbital ridge, usually on one side. The operation can then be done, as Dr. Jones says, at a much earlier date and can be carried out with removal of less bone. I do not think there should be any discussion of osteomyelitis of the skull without an expression of thanks to Dr. McKenzie of London and Dr. Furstenberg for their splendid achievements in cases of osteomyelitis of the frontal bone. I agree with both that the so-called radical operation is the one of choice and that there is no place for what is termed the "conservative" operation. With the latter there is grave danger of extension of infection, which may be complicated by formation of a brain abscess.

DR. SAMUEL R. SKILLERN JR., Philadelphia: I have never seen a self-limiting type of osteomyelitis of the calvarium. How can one rule out the presence of a subdural abscess in the so-called silent area of the brain, the frontal lobes, unless the dura over this area is exposed? The removal of the pos-

terior sinus plate usually will demonstrate a subdural abscess; if not, at least it will allow any deep collections of pus to work their way upward into the operative field. The timid operator who treats the infected calvarium certainly is running the chance of a rapidly spreading infection of the bone with the likelihood of intradural complications. When one thinks that all such risks are lowered at least 80 per cent by a wide bone resection and that a regeneration with almost a perfect contour of the calvarium can be obtained from transplants of the calvarial bone, it seems to me poor judgment to take such chances. I have modified the Mosher U incision by carrying it through the upper edge of the hair of the eyebrow, then upward into the temporal hair. This incision minimizes the scarring of the forehead. The contents of the temporal fossa are avoided by dissecting the skin forward to the superior temporal ridge before incising the deeper tissues. The vitality of this soft tissue flap is retained by encapsulating it in a hot saline towel. In several cases in which the infection had infiltrated the bone, with or without intracranial complications, any remaining postoperative infection was seemingly controlled in from ten to fifteen days by the use of a bacterial antigen. This antigen was made from Staphylococcus aureus and albus, with lysed staphylococcus and streptococcus proteins in solution. I think that Dr. Mosher is ultraconservative in his prolonged open drainage. An early closure of the wound prevents the foreshortening of the flaps, does away with the necessity of pressure bandages and allows the skull to assume its normal shape. Granting that after the closure of the wound a collection of pus occurs, a diagnosis readily can be made as it causes a localized puffy tumor of the soft tissues. I do not hesitate to reopen the entire wound by breaking the newly formed connective tissue. I have had two such cases in which healing promptly occurred without undue disfigurement after the evacuation of the pus, followed by several days of drainage through a stab wound in the replaced flap. It is such a simple surgical procedure to take thin bone chips from the calvarium and plant them in their own environment that it seems to me unnecessary to replace the lost tissues by any foreign material.

DR. CORNELIUS G. DYKE, New York: As a radiologist, I wish to emphasize the importance of obtaining roentgenograms of the frontal and maxillary sinuses in the upright position. The patient must be erect in some cases so that secretions in the frontal sinuses may be visualized, for if the film is made with the patient horizontal no fluid level is formed and no evidence of infection may be visible in the roentgenograms. The lateral view is of considerable importance, and in the relatively few cases of acute frontal osteomyelitis following frontal sinusitis that have been seen at the Neurological Institute (about one year) the lateral view when slightly underexposed may show some localized edema of the scalp or slight decalcification of the bone in ensuing osteomyelitis. It should be emphasized that the complications of acute osteomyelitis of the frontal bone secondary to frontal sinusitis are uncommon, for, as Dr. Macmillan has stated, in twenty years he has encountered only eighty-six cases at the Massachusetts Eye and Ear Infirmary; in other words, about four cases a year in an institution that has an extremely active eye, ear, nose and throat service. However, only in this kind of hospital is it possible to collect a sufficient number of cases to determine which method of treatment is the best. In how many of the last sixteen cases, in which there was a mortality of 25 per cent, had sulfanilamide or one of the related compounds been administered?

DR. HARRIS P. MOSHER, Boston: I congratulate Dr. Jones on having microscopic sight in being able to tell normal from diseased bone. I have not acquired that facility yet. His cases, to my mind, are not of the fulminating type. I am ready to change my operation technic and change in any way that the adequate experience of others dictates. Dr. King supported me from the general surgical standpoint, and I have said a few things about the lack of the general surgical principles among some specialists. I was glad to hear Dr. King say that the patient can bleed to death if one is not careful to stop the bleeding as one is turning up the flap. I would agree with what he said about obliterating the frontal sinuses. If one does not obliterate it in these cases, one is going to have trouble afterward, and the way to obliterate it is to take off both anterior and posterior walls. As Dr. Skillern says that I may be overconservative; if so, it is for him to prove it. He referred to chemotherapy. This is coming in. A note has been handed to me that sulfathiazole as a powder can be used in dressings. About Dr. Skillern's use of bone chips, this method was used in the World War and is worth trying again. Dr. MacMillan said that the x-rays were outmoded in osteomyelitis. I do not agree to that. Let me leave these thoughts with you: If you can find out which is a nonfulminating case, so much the better. Treat it accordingly. But watch the diploic veins. If one vein enlarges, showing that it is carrying infection, the bone carrying it should be removed. Especially watch the veins at the external angle of the frontal sinus. There have been some tragedies lately where these have not been watched.

DR. A. S. MACMILLAN, Boston: As Dr. Wilinsky in New York has said with regard to osteomyelitis being a limited disease, it is very often limited, but it is limited by the death of the patient. Within the last month, three cases of osteomyelitis have come in and have been treated by Dr. Champ Lyons at the Massachusetts General Hospital, in which he used heparin to prevent thrombophlebitis by increasing the clotting time, and sulfathiazole as a chemotherapeutic agent. His results in these cases, so far, have been startling, and we should watch for his paper on this subject.

DIABETES INSIPIDUS

TREATED BY THE SUBCUTANEOUS ADMINISTRATION OF A SUSPENSION OF PITRESSIN TANNATE IN OIL

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It has been known for several years that solution of posterior pituitary controls the manifestations of diabetes insipidus. The pioneer work of Farini and Ceccaroni [1] and of von den Velden [2] demonstrated the efficacy of the hypodermic administration of solution of posterior pituitary, and Blumgart [3] showed that spraying the solution into the nose was also effective. Furthermore, intranasal insufflation of the powdered whole gland controls the symptoms, as was shown by André and Lucie Choay.[4] It was found by Kamm and his co-workers [5] that pitressin contained the active antidiuretic substance.

The subcutaneous administration of solution of posterior pituitary or pitressin appears to be the most effective method of treatment. Warkany and Mitchell [6] quoted Nobécourt and Ducas's statement that it is effective in 95 per cent of the cases. Certain very disagreeable side effects, however, such as pallor, diarrhea, palpitation, headache, nausea, intestinal cramps and increased blood pressure often occur. These side effects and the necessity of giving the injections very frequently make the prolonged use of such therapy impracticable.

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Nasal insufflation of the powdered whole gland is often more convenient and less painful, but in the severe case it may be required from six to eight times a day and at least one time during the night.

Methods to produce slow absorption of hormones have been shown to be desirable in certain endocrine deficiencies. It seems to us that diabetes insipidus is such a disease. We have been able to find only two reports of efforts to prolong the effect of the antidiuretic principle of the posterior pituitary gland. Wankmüller [7] administered hypodermically a posterior pituitary preparation dispersed in vegetable and animal oil to three patients with diabetes insipidus. A single injection controlled the symptoms for from three to five days. The injection twice a week of 1 cc. of a water-in-oil emulsion of concentrated liquid pituitary extract prepared by Court and Taylor [8] controlled the symptoms in one case.

The present report is concerned with the effect of the subcutaneous administration of pitressin tannate suspended in oil,[9] on three cats with experimentally produced diabetes insipidus,[10] on two patients with the idiopathic form of diabetes insipidus and on one with diabetes insipidus which was thought to be a manifestation of lipoid granuloma. Pitressin tannate is a water-insoluble chemical combination of a pressor fraction of the posterior lobe of the pituitary gland with tannic acid. The pressor fraction is precipitated with tannic acid, and the precipitate is removed by filtration and washed and dried, all under aseptic conditions. Five pressor units of pitressin tannate are suspended in each cubic centimeter of peanut oil. The p_H of the solution is that of oil. The antidiuretic effect is one of the subjects of this report. In the cats, only the effect on the urinary output and specific gravity was ascertained, but in the patients the effect on the fluid intake, urinary output and specific gravity, blood pressure and urea clearance was studied.

TABLE 1.—*Effect of 1 Cc. of Pitressin Tannate in Oil on Cats with Experimentally Produced Diabetes Insipidus*

	Control			1			2		
Cat	No. Days	Average Output, Cc.	Average Specific Gravity	Days Active	Average Output, Cc.	Average Specific Gravity	Days Active	Average Output, Cc.	Average Specific Gravity
1	7	429	1.006	3	210	1.019	4	162	1.024
2	7	506	1.008	5	143	1.030	4	162	1.026
3	7	856	1.004	3	187	1.025	3	228	1.020

TABLE 2.—*Total Duration of the Effect of 1 Cc. of Pitressin Tannate in Oil on a Cat with Experimentally Produced Diabetes Insipidus*

Control: Average urine output, 856 cc.
Average specific gravity, 1.004

3/14/40: Pitressin tannate in oil, 1 cc.

	Urine, Cc.	Specific Gravity
3/14/40	780	1.015
3/15/40	200	1.030
3/16/40	135	1.025
3/17/40	225	1.020
3/18/40	525	1.003
3/19/40	650	1.004
3/20/40	700	1.005

It is to be noted from table 1, which shows the effect of the subcutaneous administration of the material to cats, that an injection reduced the urinary output and increased the urinary specific gravity for from three to five days. Sufficient time was allowed between injections for the urinary output and specific gravity to return to the control level. Actually the effect was even more prolonged, as demonstrated in table 2, which shows the daily urinary output and specific gravity in the case of cat 3 of table 1, following the administration of pitressin tannate in oil. The rise in specific gravity during the first day was greater than the decline in the urinary output, whereas, as the effect subsided, the specific gravity declined more rapidly than the urinary output increased. Some effect was demonstrable, therefore, in this animal for seven days, although the maximum effect occurred for only three days. The same was true for the other animals, although to a lesser degree.

TABLE 3.—*Comparative Effect of No Therapy, Intranasal Insufflation of Powdered Whole Gland, and Pitressin Tannate in Oil on Patient 1*

Experimental Period	No. Days	Average Intake, Cc.	Average Output, Cc.	Average Specific Gravity	Urea Clearance	Average Blood Pressure
No therapy	3	13,170	13,815	1.000	67%	115/70
Powdered whole gland, 25 mg. 4 times daily by intranasal insufflation	5	1,930	1,380	1.013	101%	116/60
Pitressin tannate in oil, 1 cc. every other day	8	1,430	1,155	1.021	158%	110/60

TABLE 4.—*Comparative Effect of No Therapy, Solution of Posterior Pituitary, Pitressin and Pitressin Tannate in Oil on Patient 2*

Experimental Period	No. Days	Average Intake, Cc.	Average Output, Cc.	Average Specific Gravity	Urea Clearance	Average Blood Pressure
No therapy	4	11,300	11,925	1.000	132%	120/80
Posterior pituitary solution, 1 cc. twice daily	2	4,200	5,250	1.004	.....	120/60
Pitressin, 1 cc. twice daily	5	3,600	3,355	1.006	.....	120/66
Pitressin, 1 cc. three times daily	5	2,440	2,520	1.010	.....	126/76
Pitressin tannate in oil, 1 cc. every other day	9	2,725	2,970	1.013	118%	126/66
Pitressin tannate in oil, 1.5 cc. every other day	8	2,410	2,065	1.018	138%	128/60

Of the patients observed, the first was a boy 16 years of age whose symptoms had been controlled previously by hypodermic injections of solution of posterior pituitary and later by the intranasal insufflation of 25 mg. of the powdered whole gland four times daily. The daily urine volume during insufflation treatment varied from 2,000 to 3,000 cc., and the specific gravity from 1.010 to 1.015. It is to be noted from table 3, which compares the effect of intranasal insufflation of the powdered whole gland with subcutaneous administration of pitressin tannate in oil on this patient, that the manifestations were better controlled with the latter method of treatment. Not shown in the table is the duration of the effect of the administration of 1 cc. of this material. This varied from forty-eight to eighty-two hours and averaged fifty-seven hours. During the eight days of treatment covered by table 3, injections were repeated before the complete disappearance of the effect of the previous one. After the patient left the hospital the injections were repeated only as often as necessary to control his symptoms. He reports that

7. Wankmüller, R.: Effectiveness of Tonephen (Posterior Pituitary Preparation) Administered Parenterally in Depot Form in Diabetes Insipidus, Klin. Wchnschr. **18**: 566 (April 22) 1939.
8. Court, Donald, and Taylor, S. A.: Diabetes Insipidus Treated by Slowly Acting Pituitary Emulsion, Proc. Roy. Soc. Med. **32**: 1203 (Aug.) 1939.
9. Supplied by Parke, Davis & Co.
10. Available through Dr. W. R. Ingram, Department of Anatomy, State University of Iowa College of Medicine.

1 cc. is required every sixty to seventy-two hours. There were no side effects from the use of pitressin tannate in oil, although the manifestations of the syndrome were controlled more completely. The arterial pressure was not increased but there was an apparent increase of the urea clearance.

The second patient was a boy aged 17 years who was refractive to the intranasal insufflation of the powdered whole gland even when as much as 200 mg. was administered at one time. His symptoms were adequately controlled by an injection of 1 cc. of solution of posterior pituitary every twelve hours. The resulting headache, however, was so pronounced that after one year he discontinued the drug. The effect of administering solution of posterior pituitary hypodermically in 1 cc. doses two times a day, and of pitressin in 1 cc. doses two and three times a day, compared with the effect of administering pitressin tannate in oil in 1 and 1.5 cc. doses every other day, is shown in table 4. The effect of 1 cc. of pitressin tannate in oil lasted from thirty to fifty-three hours and averaged forty-four hours. The duration of the effect was not noticeably prolonged by increasing the dose to 1.5 cc. but the symptoms were better controlled. The symptoms were as well controlled when pitressin tannate in oil was administered every other day as when three injections of pitressin were given daily. There was no appreciable effect on the blood pressure or urea clearance, and headache did not occur. After the patient left the hospital the symptoms were controlled satisfactorily by an injection of 1 cc. every forty-eight to fifty-two hours.

The third patient was a woman aged 39 who was also refractive to the intranasal insufflation of the powdered whole gland, but her symptoms were well controlled by the injection of 1 cc. of solution of posterior pituitary every twelve hours. Pallor, nervousness and the passage of several watery stools frequently followed an injection. The results of the use of pitressin tannate in oil are shown in table 5. The duration of the effect of 1 cc. varied from thirty-two to forty-four hours and averaged thirty-seven hours, whereas 2 cc. prolonged the effect to from sixty-four to sixty-eight and one half hours. A very disagreeable sense of "uneasiness" was experienced following the administration of 2 cc. Unfortunately, no measurements of the blood pressure were made during this period of study. No disagreeable side effects were noted after a dose of 1 cc. and there was no appreciable effect on the blood pressure or urea clearance.[11]

TABLE 5.—*Effect of Pitressin Tannate in Oil on Patient 3*

Experimental Period	No. Days	Average Intake, Cc.	Average Output, Cc.	Average Specific Gravity	Urea Clearance	Average Blood Pressure
No therapy.....	3	6,530	7,280	1.001	82%	130/80
Pitressin tannate in oil, 1 cc.	9	2,060	1,130	1.022	97%	118/76
Pitressin tannate in oil, 2 cc.	7	2,060	1,470	1.021	88%	.....

The viscosity of the oil at room temperature requires that the ampule be immersed in warm water for several minutes and thoroughly shaken before the material is withdrawn into the syringe. It is preferable to use a 20 gage needle for filling the syringe and an ordinary hypodermic needle for the injections. There was no reaction at the site of the injections. Nevertheless it is advisable to vary the site of the injections. The patients were easily taught to administer the preparation themselves.

11. Since this paper was submitted for publication, two additional patients with idiopathic diabetes insipidus have been treated. The first was a 17 year old girl and the second a 24 year old man. In the first case the symptoms were controlled for from fifty-one to sixty-eight and one half hours (average, fifty-six hours) by 1 cc. of pitressin tannate in oil and, in the second, for from fifty to seventy hours (average, fifty-five hours).

SUMMARY

Pitressin tannate in oil was administered to three patients with diabetes insipidus and to three cats with experimentally produced diabetes insipidus. The duration of the effect was ascertained, and the efficacy of this method of treatment was compared with that of other preparations of the posterior pituitary gland.

The duration of the effect in the cats varied from three to seven days, and in the patients from thirty to eighty-two hours. The effect on the manifestations of the disease in the patients was equal to that of other preparations of the posterior pituitary gland and there were no disagreeable side effects.

THE CHEMICAL AND MECHANICAL PREVENTION OF SYPHILIS AND GONORRHEA

PRELIMINARY STATEMENT BY THE SPECIAL JOINT COMMITTEE APPOINTED BY THE AMERICAN SOCIAL HYGIENE ASSOCIATION AND THE UNITED STATES PUBLIC HEALTH SERVICE

H. H. HAZEN, M.D., WASHINGTON, D. C., CHAIRMAN; IRA V. HISCOCK, C.P.H., Sc.D., NEW HAVEN, CONN.; P. S. PELOUZE, M.D., PHILADELPHIA; WILLIAM F. SNOW, M.D., NEW YORK; HANS ZINSSER, M.D., BOSTON; RAY H. EVERETT, L.L.B., WASHINGTON, D. C., SECRETARY.

The Committee was requested to review the history and present status of the prevention of syphilis and gonorrhea by chemical and mechanical means and to make such recommendations as seemed desirable at the present time. The Committee has had several meetings in New York and Washington, has reviewed the published material dealing with its field of study and has heard testimony from representative members of the Army Medical Corps, the Navy Medical Corps, the United States Public Health Service, state health officers, the medical profession, representatives of Negro medical and public health groups, medical schools, voluntary health organizations, religious organizations, educational organizations, social welfare agencies and civic organizations.

The Committee is cognizant of the fact that chemical and mechanical prophylaxis is only one phase of preventive medicine. The prevention of syphilis and gonorrhea by chemical or mechanical means is supplementary to and not a substitute for the prophylaxis of these diseases by educational measures which employ ethical and religious motives. Nor does chemical or mechanical prophylaxis justify any relaxation of efforts to reduce to a minimum exposure to infection by discouragement of prostitution and other forms of sexual promiscuity. In the case of syphilis and gonorrhea, as with other communicable diseases, the best and surest method of prevention of infection is the avoidance of exposure. Educational, religious, sociologic and legal activities which tend to prevent exposure to infection are of great importance. At the same time, however, the Committee is fully aware of the fact that sexual promiscuity is a very important factor in their

Dr. Zinsser died, September 4.

spread. To decrease the number of carriers among this group of men and women, chemical and mechanical prophylaxis is necessary and hence is complementary to educational measures.

The place of chemical and mechanical preventive measures is at the point where educational, religious, social and legal efforts have failed to prevent exposure to infection. At that point preventive medicine offers reasonably efficient methods of prevention, which, if correctly applied, will in the majority of instances prevent the exposed person from becoming infected and from becoming a possible source of infection to those with whom he may later have contact. Thus not only one individual but that individual's family and community may be relieved of the burdens—medical, social and economic—of syphilis and gonorrhea. The employment of chemical and mechanical prophylaxis will preserve the efficiency of men required for defense or service of the nation in time of peace or of war. This being the case, it becomes the moral obligation of sanitarians to urge the wide dissemination of all available knowledge regarding such procedures.

After carefully reviewing the available scientific data as to the efficiency of various means of chemical and mechanical prophylaxis, the Committee makes the following specific recommendations:

THE CHEMICAL AND MECHANICAL PREVENTION OF SYPHILIS AND GONORRHEA [1]

1. Safest method.
   - A. Use a condom of standard type.
   - B. Thoroughly wash the genitals and adjacent parts with soap and water as soon as possible (the sooner the better, but within one hour at most) after removal of the condom.
2. In the absence of a condom.
   - A. Thoroughly wash with soap and hot water as already described.
   - B. After urination, inject 6 cc. of 2 per cent strong protein silver solution, or other efficient, nonirritating germicidal solution into the urethra and hold for five minutes.
   - C. Rub 33 per cent ointment of mild mercurous chloride (calomel ointment) into the genitals and adjacent parts.

COMMENT [2]

The habit of cleanliness materially reduces the risk of infection. For the proper application of 2 B and C, skilled attention and use of a syringe are necessary. Prophylactic treatment of this type can be given by physicians, by some clincis, and in prophylactic stations where they exist.

The Committee emphasizes the fact that the foregoing suggested preventive measures are not 100 per cent successful. Their efficacy depends first on the reliability of the materials used. A defective condom does not give the same degree of protection as a sound article. The strong protein silver solution or the mild mercurous chloride may not be of the proper strength or may be inactive. Second, washing and application of chemicals may be delayed too long after exposure. Drunkeness may prevent correct application of any of these methods. It may be stated, however, that when these methods are followed correctly they will in the majority of instances prevent infection with syphilis or gonorrhea.

The medical profession and public health agencies, both official and voluntary, bear a heavy responsibility in the matter of the prevention of syphilis and gonorrhea by chemical and mechanical means. Since these methods are efficacious they would, if widely understood and correctly utilized by those who expose themselves to the danger of infection, result in a great diminution of syphilis and gonorrhea and would thereby greatly reduce personal, family and community disasters and the economic losses that result from these infections.

It seems clear, therefore, that health education with regard to syphilis and gonorrhea should include simple, frank and explicit directions as to chemical and mechanical prophylaxis. This information should be included in its proper setting and in appropriate language.

It seems apparent also that, in addition to instructing the public regarding this preventive medical method, civilian, military and naval, medical and health authorities have the obligation to provide the facilities through which chemical and mechanical prophylaxis may be made available when and where needed. The authorities also have the responsibility for preventing the commission of fraud through the sale of worthless products to the public for the prevention of these diseases.

Finally the Committee is impressed with the fact that there are many unsolved and administrative problems within the scope of chemical and mechanical prophylaxis and the provision of adequate facilities for these procedures. It is considered that research in this field should be continued.

1. The directions for the prevention of syphilis and gonorrhea apply to the prevention of all other venereal diseases as well.
2. In this initial report the Committee has purposely avoided going into detail, believing that only general principles should be discussed. In the full report detailed methods will be given at length.

Clinical Notes, Suggestions and New Instruments

ASPIRATION OF SPUTUM FROM ADULTS

W. J. AUGER, M.D., TORONTO

During the past three years a new aspiration method of obtaining sputum at the Hospital for Sick Children has been in use. With one attempt it is usually possible to obtain sufficient sputum from the larynx or nasopharynx for direct examination and cultural purposes. The apparatus consists of a glass syringe, a catheter and a simple valve arrangement which permits powerful intermittent suction. By use of this method it has been learned that in children the nasopharynx is an ideal source for obtaining sputum for typing pneumococci in early cases of pneumococcic pneumonia, while sputum from the larynx is more suitable for examination in cases of tuberculosis, whooping cough or pneumonia due to a mixed infection.[1] The type of pneumococcus found in the nasopharynx has agreed in most cases with the type found in exudates, blood cultures and lung cultures at postmortem examination whenever these examinations have been possible. The only difficulty with this method is that in about 12 per cent of cases two types of pneumococci are to be encountered on direct examination, one type probably acting in the role of pathogen. Occasionally three types are to be found.

In view of these observations a study was made of expectoration of pneumonia patients among adults at the Toronto General Hospital through the courtesy of Dr. Duncan Graham. There were two objectives: The first was to learn whether sputum was obtainable from those patients who said that they could not cough or expectorate. This is frequently the case when the patient is too weak or irrational. Too often the

Working under a grant from the Banting Research Foundation in pneumonia research in the Department of Pathology and Bacteriology at the Hospital for Sick Children.

1. Auger, W. J.: An Original Method of Obtaining Sputum from Infants and Children with Reference to the Incidence of Pneumococci in the Nasopharynx, J. Pediat. **15**: 640 (Nov.) 1939.

technician complains to the intern that the specimen received was not expectorated but was salivated. The latter problem is of interest in the study not only of pneumonia but also of tuberculosis. The second objective was to learn whether secretion from the nasopharynx would yield large numbers of pneumococci as in children and whether this method of obtaining sputum offered any short cut in the early diagnosis of pneumococcic pneumonia.

METHOD

Thirteen patients with pneumonia from the wards of the Toronto General Hospital were chosen over a period extending from April 1 to May 30, 1939. These were patients from whom the intern in charge was unable to obtain any sputum or, if he did, the sputum obtained was found in the laboratory to be unsuitable for direct examination. On notification of such cases, I attended the patient and obtained specimens of secretion from both the larynx and the nasopharynx by the aspiration method. The sputum was examined directly by smear and for the quellung phenomenon. It was then cultured on a blood agar plate, carbon dioxide being used.[2] (The mouse cultural method was not used.)

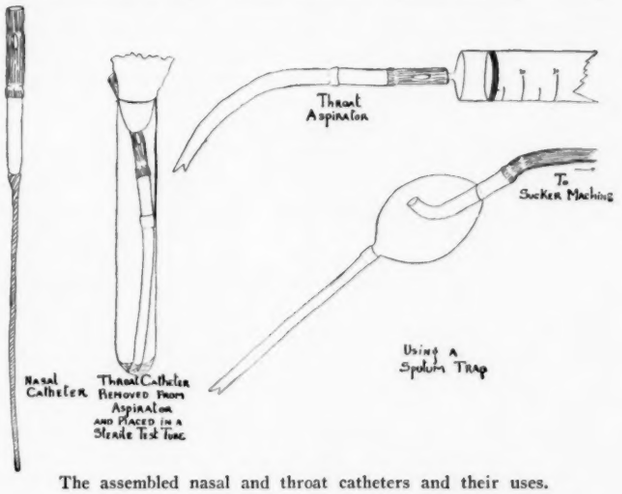
ASPIRATION METHOD

The construction and operation of an "aspirator" has already been described in a pediatric journal;[1] a short review will be presented here. The operation is essentially the same for adults except that more cooperation is expected, and the assistance of a nurse is not usually necessary. The apparatus consists of a 50 cc. syringe, a 2 inch piece of soft rubber tubing of three-sixteenths inch inside diameter with a small hole cut in one side (to act as a simple finger valve), a 2 inch piece of glass tubing of one-fourth inch outside diameter to act as an indicator for the sputum, and a catheter designed for either nasal or pharyngeal passage (see diagrams). All these materials can be obtained in any hospital supply room.

By the nasopharyngeal method the catheter (a number 9 or 10 French catheter) is inserted into the nasopharynx until it is judged to be in the "adenoid" area. Suction is commenced by having the operator hold the barrel of the syringe in the left hand and with the forefinger cover the window of the soft rubber tubing which connects the syringe with the glass tubing. The piston of the syringe is withdrawn with the right hand. At the end of the outstroke the finger is removed from the hole in the rubber tubing and the piston is shoved back into the syringe. In this manner the air is short circuited and the sputum is not returned into the nasopharynx. After repeated intermittent suction in this manner, the sputum will be seen to rise into the glass connection. Then the catheter is removed from the nose and placed in a sterile test tube. The sputum is forcibly ejected into the test tube by reversing the process, namely the forefinger covers the valve on the instroke of the piston and is removed on the outstroke. The thumb and forefinger of the right hand should grip some of the piston beyond the handle to prevent driving the piston through the end of the barrel during the process of ejection. The catheter is left in the test tube and is taken to the laboratory for further examination. The nasal method can be used to obtain sputum from the larynx, but the bore of the catheter is small and liable to be obstructed by thick sputum.

The laryngeal method employs a catheter of fairly stiff rubber tubing 4 by 5 inches long and of one-eighth inch inside diameter with a notched tip. This catheter allows for the collection of large amounts of sputum. The suction principle is essentially the same as in the nasopharyngeal method but is performed faster and more energetically. Some experience is required on the part of the operator to achieve best results. The patient is asked to open his mouth and cough. With the operator holding the syringe and valve in the left hand, the right hand at first directs the catheter to the base of the tongue while the patient is coughing. When the catheter is in position with its tip at the base of the tongue and above the opening of the larynx, the right hand changes position and pulls and pushes the piston as in the nasopharyngeal method. When the catheter is heard to "catch" on the expectoration or when sputum is seen to rise into the glass connection, the catheter is removed and the sputum ejected into a sterile test tube. This procedure may have to be repeated before sufficient sputum can be obtained. This method is more irritating to the patient but at the same time one is sure that the sputum has come from the larynx or the trachea. In some cases the catheter does not catch any sputum but the patient is able to expectorate afterward, owing to the irritation of the cough reflex. This method should be done about two hours after meals. A cellophane mask covering the face should be worn by the operator.

A simpler method of aspirating sputum from the larynx is to use a sputum trap in conjunction with a machine suction apparatus. The sputum trap is constructed of an obstetric bulb with a 5 to 6 inch throat catheter attached to its lower end and the tube from a suction machine to the upper end. The catheter is directed to the back of the throat with the right hand, the left hand being left free to use a tongue depressor (the operator standing to the right of the patient). The sputum is aspirated in large quantities into the glass obstetric bulb and is removed from the bulb in the laboratory by attaching syringe and finger valve to the upper end and drawing and expelling saline solution in and out of the bulb. This method requires little experience, and its only disadvantage is in the requirement of a cumbersome machine suction apparatus. One distinct advantage of this technic, however, is that it leaves the left hand free to retract the tongue, so that the right hand can more accurately direct the tip of the catheter. This method has only recently been devised and used but has so far proved very satisfactory.


Throat Aspirator
To Sucker Machine
Using a Sputum Trap
Nasal Catheter
Throat Catheter Removed From Aspirator and Placed in a Sterile Test Tube

The assembled nasal and throat catheters and their uses.

RESULTS

A comparison of the secretions from the nasopharynx with those from the larynx of thirteen adults with pneumonia was made. No conclusions were drawn as to the probable etiology of the respective pneumonias because of the small number in the series. The pathogenic bacteria recorded merely indicated their presence in nasal and laryngeal secretions.

In only two cases was the patient totally unable to expectorate voluntarily. In the other cases the sputum was insufficient because it consisted more of saliva than of purulent matter. In these cases the adult resembles the child and confuses expectoration with salivation. But, with the aspiration method, sputum with a minimum of saliva was always obtainable in all thirteen cases whether the nasal or the laryngeal route was used. The sputum was always sufficient for direct smear, Neufeld test and cultural methods.

The laryngeal method seems to be the easiest and most satisfactory for obtaining large amounts of sputum, particularly when the patient is weak or irrational. This is in contrast to children, in whom the nasopharynx is usually full of purulent secretion. It may be explained by the fact that the adult is uncomfortable whenever there is nasal obstruction and is continually blowing

2. Auger, W. J.: A New Method of Culturing Sputum on Solid Media Using Carbon Dioxide for the Isolation of Pneumococci, Brit. J. Exper. Path. **20**: 439 (Dec.) 1939.

his nose or clearing his nasopharynx to rid himself of this feeling. Because large amounts of sputum relatively free from saliva were obtained from the larynx in patients when voluntary expectoration had failed, this method is recommended for getting suitable sputum from tuberculous patients. The laryngeal method has been particularly useful in infants and children in this respect.

In only one case were pneumococci more numerous in the nasopharyngeal secretions than in the laryngeal. There were eight cases of pneumonia with pneumococci in the sputum. In most cases the type of pneumococcus or other pathogenic bacteria found in the back of the nose agreed with that found in the larynx and also in about equal numbers. In children, on the other hand, in cases of early pneumococcic pneumonia, the nasopharyngeal secretions have been found to contain larger numbers of pneumococci than the laryngeal secretions.[1] This may be due in part to the relative absence of adenoid tissue in the adult. It is felt however that, if a stiff catheter with a curve to reach the roof of the nasopharynx could be constructed and inserted, perhaps foci of infection in the sinus recesses of the adult nose would yield interesting information. The secretions from the nose were usually freer of mouth organisms than laryngeal secretions. This is due to the throat aspirator unavoidably picking up mucus from the back of the throat. However, this can be partially remedied by careful washing of the sputum. In one case no likely etiologic organisms were isolated. The patient had received sulfapyridine for thirty-six hours before the sputum was aspirated. This illustrates the value of obtaining sputum before chemotherapy is started.

COMMENT

This study is admittedly based on a small number of cases and no conclusions should be made without further trial; nevertheless the ease with which large amounts of sputum could be aspirated from the larynx of patients who found it difficult to expectorate voluntarily seemed to justify the publication of this method. Since considerable bacteriologic experience is necessary for the examination of the sputum and some practical experience is required to operate the laryngeal aspirator, it is recommended that one person should both obtain and examine the sputum. This is to insure that suitable sputum reaches the laboratory.

With the advent of chemotherapy in the treatment of pneumonia there is a tendency to ignore sputum examination. While sulfapyridine may be administered without regard to the type of pneumococcus, for prognostic evaluation the type of pneumococcus may be of significance. In cases of streptococcic pneumonia sulfanilamide may be the drug of choice. In cases of pneumonia due to a staphylococcus or to Bacillus influenzae, the treatment and outlook are uncertain. This would indicate that early sputum examination is essential for prognosis and research in the treatment of pneumonia. On the other hand, proper sputum is essential for laboratory examination. A direct smear from purulent matter can in most cases anticipate the results from the cultures. Much time and labor may be saved in the laboratory by care in obtaining sputum at the bedside.

SUMMARY

A brief study was carried out on thirteen adults with pneumonia who reputedly could not cough or bring up satisfactory sputum for examination.

In all thirteen cases sufficient sputum was obtainable from either the larynx or the nasopharynx by the use of the aspiration method.

No advantage was found in nasopharyngeal secretions as compared with secretions from the larynx in the typing of pneumococci in pneumonia among adults.

The laryngeal aspiration method of collecting sputum, whether obtained by syringe and finger valve or by a sputum trap and machine suction, has been suggested for adults when voluntary efforts at expectoration have failed. This method is also recommended for obtaining sputum from tuberculous patients.

It is suggested that the person who examines the sputum in the laboratory should obtain the sputum.

ACUTE INFECTIOUS POLYNEURONITIS FOLLOWING PNEUMONIA

ALEXANDER LEON LOURIA, M.D., AND HARRY MANDELBAUM, M.D.
BROOKLYN

A rapidly extending paralysis ultimately involving all four extremities in a flaccid paralysis developed suddenly on the fourth day following the crisis of an uneventful case of bronchopneumonia. This infrequent sequel, difficult of recognition at its inception, is hereby reported:

REPORT OF CASE

History.—S. B., a boy aged 16, who entered the Jewish Hospital of Brooklyn on Dec. 4, 1938, had always enjoyed good health except for an uncomplicated scarlet fever at the age of 10. Six days before entering the hospital he complained of headache, weakness and lassitude. The temperature rose to 104 F. and he began to cough without expectoration. There was no chill. The temperature ranged between 100 and 104 F. daily. The day before admission to the hospital, he complained of pain in the left side of the chest on deep breathing and on coughing.

Examination.—On admission the patient was well developed and did not appear very ill; there was no dyspnea, cyanosis or jaundice. The pharynx was deeply injected; the tongue was moist and slightly coated. Some impaired resonance to percussion was obtained below the angle of the left scapula, and moist rales were evident at the end of inspiration at this site. The heart appeared normal, the abdomen was soft and the viscera were not palpable. There was no nuchal rigidity, no alteration of the tendon or superficial reflexes, no sensory changes and no cranial nerve palsies.

Course.—The temperature ranged between 102 and 103 F. daily. There was not much cough and occasionally he would raise a thick grayish sputum. Repeated examinations of the sputum showed no pneumococci; no hemolytic streptococci were obtained on culture; nondescript, indifferent streptococci were found. On the second day following his admission, dulness, bronchial breathing and many crepitant rales were noted in the right axilla and right interscapular region. The left lung was clear. X-ray study at this time showed bronchopneumonic infiltration of the base of the right lobe. Epistaxis occurred on the second and third day of his hospital stay.

In the absence of any specific typing and because no disturbing symptoms had arisen, he was given no specific medication, nor had any medication been taken before admission. The elevation of temperature continued for four days; on the fifth day it precipitately dropped from 103.4 F. to normal, and it remained normal thereafter. Blood counts during this period showed a red blood cell count of 4,800,000 and a leukocyte count of 9,000; there were 60 per cent polymorphonuclear cells, 20 per cent band forms and 20 per cent lymphocytes. Urine examinations showed no pathologic features.

Four days after the temperature had dropped to normal (fifteen days after the onset of pneumonia) he suddenly found himself unable to raise his arms sufficiently to feed himself. Examination showed weakness of both arms, especially the proximal muscle groups. The grip of each hand was diminished; the left was involved to a greater extent than the right. The following day it was noted that the pupils were irregular; they reacted promptly to light and in accommodation. The eyegrounds showed slight haziness of the disks. Slight lateral nystagmus was present, but it was easily exhausted. There was definite weakness of all four extremities, more marked in the shoulder and pelvic girdles. All the deep reflexes were lost. The cremasteric and abdominal reflexes were lost. There were no alterations in sensation or muscle tenderness. The patient did not complain of pain.

A spinal tap was performed on December 15 (two days after the onset of the paralysis). The initial pressure was 110 mm. There was a sharp rise and fall of the initial pressure with successive straining, jugular pressure and abdominal pressure; 8 cc. of spinal fluid was removed. It appeared crystal clear. There were 8 lymphocytes; the Wassermann and colloidal gold tests were negative; the chemical analysis showed a total protein

From the medical service of Dr. Louria, the Jewish Hospital.

of 42 mg. and a sugar content of 63 mg. per hundred cubic centimeters. No organisms were grown on culture of the spinal fluid. The following day, December 16, he complained of pain in both shoulders and arms and numbness and tingling of both hands. But little voluntary action remained in the extremities. The palate was noted to deviate slightly to the left, but this cleared in two days. At this time some pharyngeal weakness was evident as well as some weakness of the right facial muscles. Tests for electrical reactions of degeneration (faradic current) were performed on all muscles and were found within normal limits.

During the following week he complained of considerable pain in both arms and shoulders; some atrophy was now apparent in most of the muscles but appeared to be most marked in the hands. No fibrillary twitchings were noted. The pharyngeal weakness and the slight facial palsy cleared by the end of the third week.

On January 7, twenty-five days after the onset of the paralysis, the pain in both shoulders and arms was less. He was mentally clear. There was no nuchal rigidity; the pupils were slightly irregular. The eye grounds were normal; there were no cranial nerve palsies. Some muscle tenderness was noted. There were no fibrillary twitchings; muscular atrophy was slightly more marked. The tendon reflexes of the upper extremities and the abdominal reflexes were gone, the cremasteric reflexes and tendon reflexes of the lower extremities had returned to normal. There were no sensory disturbances. At no time was there any loss of sphincteric control. An orthopedic examination at this time revealed the following details: In the right upper extremity there were some atrophy of the deltoid, marked weakness of the external rotators and moderate weakness of the internal rotators of the arm; the triceps and the biceps action were reduced 50 per cent; there was marked loss of dorsiextension at the wrist; flexion at the wrist was good; there were complete loss of extension of the fingers and marked weakness of the flexors of the fingers. In the left upper extremity there were marked weakness and some atrophy of the shoulder and arm; the external rotators were almost completely paralyzed but the internal rotators functioned about 60 per cent normally; the biceps and the triceps functioned about 40 per cent of normal. There were complete loss of extension of the fingers and considerable loss of flexion of the fingers. The lower extremities showed a slight degree of atrophy; flexion of the thighs was weak, abduction and adduction were good; the function of both knees and ankles was good; bilateral pes cavus was evident; the toes were retracted.

Subsequent Course.—Improvement progressed slowly. After the sixth week he no longer complained of pain, although some muscle tenderness was still evident. During the seventh week he was able to sit in a chair; during the following week he could walk with assistance. He was discharged on Feb. 5, 1939, for convalescent care and rehabilitation. At the end of the third month he was again able to feed himself and walk without assistance.

Treatment.—Twenty-four hours after the onset of paralysis, thiaminehydrochloride therapy was begun; he received 6.6 mg. intramuscularly four times daily for the first ten days; for the next two months he received a similar dose by mouth four times a day. A trial course of triple typhoid vaccine was given without appreciable benefit. The orthopedic consultant fitted him with appliances to prevent deformities until recovery was complete.

Diagnosis.—Among the diagnoses considered, the most probable were acute anterior poliomyelitis and acute infectious polyneuronitis. The sudden appearance of flaccid paralysis involving the extremities was suggestive of poliomyelitis. However, the absence of fever, leukocytosis and constitutional symptoms, the absence of pleocytosis in the spinal fluid, the symmetry of the paralysis in contrast to the patchy asymmetry of the paralysis of poliomyelitis, and finally its duration beyond the period where poliomyelitis usually halts, served to rule out poliomyelitis.

COMMENT

Acute infectious polyneuronitis, also called acute infectious polyneuritis, was originally described by Sir William Osler[1] in 1892. However, it was not accepted as an entity until the World War, when successive reports appeared in the literature (Patrick,[2] Kennedy,[3] Bradford, Bashford and Wilson[4]).

While the etiology is not known, the theory of a virus as the responsible cause finds considerable favor—a virus with a predilection for the peripheral neuron. Wilson[4] and his co-workers isolated a virus and transmitted the disease to monkeys. In a large number of cases there was a history of a preceding infection. In the thirty-five cases reported by Gilpin, Moersch and Kernohan,[5] 50 per cent had a preceding infection of the upper respiratory tract or influenza.

The essential pathologic change is a patchy degeneration of the myelin sheath of the peripheral nerve, with fragmentation of the axis cylinder and with no evidence of inflammation. The dorsal root ganglions may show lymphocytic invasion.[5] Pathologic changes on rare occasions occur in the anterior horn cells and in the brain[6] but the cord changes never resemble the lesions of anterior poliomyelitis.[7] Cobb and Coggeshall[8] summarily state that the axon seems to be more severely involved than the nerve cell, which obviously does not die and permits subsequent regeneration to take place.

During the clinical course, following recovery from a transitory infection, usually involving the upper respiratory tract, there is a latent period ranging from a few days to several months during which there are no premonitory symptoms. Then suddenly weakness and paresthesias of the extremities appear, the lower more often than the upper limbs being the site of involvement. There are no constitutional symptoms and no fever. Characteristically there is a rapid widespread involvement of all the extremities causing a flaccid paralysis of varying degree of severity. The facial nerve not infrequently becomes involved, unilaterally or bilaterally.[2] The deep reflexes are diminished or lost. Sensory symptoms are not marked, objective sensory changes are usually lacking and sphincteric control is usually not disturbed. Involvement of the cranial nerves other than the seventh is rare. No fibrillary twitchings are noted in the involved muscles. Atrophy, when it occurs, is the result of disuse.

McIntyre[9] separated the cases into four groups; group I A, with rapid onset and rapid recovery; in these cases there frequently was seventh nerve paralysis; group II A, which ran a steady down hill course with early death; group III, with a long drawn out course and ultimate incomplete recovery; and group IV, which slowly progressed to ultimate death from bulbar involvement. In most of the cases satisfactory recovery takes place within six months or a year. In the cases reported by Bradford, Bashford and Wilson[4] the mortality rate was 26.6 per cent.

The laboratory is of assistance in establishing the diagnosis. The spinal fluid is clear, not under increased pressure, shows no pleocytosis and characteristically shows an increase in the total protein. Madigan and Marietta[6] observed the changes of the protein content of the spinal fluid in a case; the initial spinal fluid showed a total protein of 18.4 mg. per hundred cubic centimeters; it increased gradually to 122 mg., then gradually declined to normal (from 15 to 45 mg.). In all the cases reported by Gilpin, Moersch and Kernohan[5] the total protein was elevated (from 100 to 1,800 mg. per hundred cubic centimeters) and the cells varied from 1 to 80, all lymphocytes.

SUMMARY

On the fourth day following the crisis of an uneventful case of bronchopneumonia, there suddenly appeared paralysis of the upper extremities. This was quickly followed by involvement of the lower extremities, with flaccid paralysis of all four

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3. Kennedy, Foster: Infective Neuronitis, Arch. Neurol. & Psychiat. **26:** 621 (Dec.) 1919.

4. Bradford, J. R.; Bashford, E. F., and Wilson, J. H.: Acute Infective Polyneuritis, Quart. J Med. **12:** 88 (Oct.) 1919.

5. Gilpin, S. F.; Moersch, F. P., and Kernohan, J. W.: Polyneuritis; Clinical and Pathologic Study of Special Group of Cases Frequently Referred to as Instances of Neuronitis, Arch. Neurol. & Psychiat. **35:** 937 (May) 1936.

6. Madigan, P. S., and Marietta, S. W.: Polyradiculoneuritis with Report of a Case, Ann. Int. Med. **12:** 718 (Nov.) 1938.

7. Garvey, P. H., and Slavin, H. B.: Acute Infectious Polyneuritis; Internat. Clin. **4:** 38 (Dec.) 1938.

8. Cobb, Stanley, and Coggeshall, H. C.: Neuritis, J. A. M. A. **103:** 1608 (Nov. 24) 1934.

9. McIntyre, H. D.: Infective Neuronitis, Ohio State M. J. **33:** 875 (Aug.) 1937.

extremities. Facial palsy developed on the right, and some edema of the optic disks was noted. There was no temperature elevation, no constitutional symptoms and no leukocytosis. The spinal fluid was clear, not under increased pressure, showed no pleocytosis and had a total protein content of 42.8 mg. per hundred cubic centimeters early in the course of the disease. There were complete loss of the deep reflexes and no objective sensory changes. Recovery was slow but progressive.

99 Lafayette Avenue.

Special Clinical Article

SULFANILAMIDE IN SURGICAL INFECTIONS

ITS POSSIBILITIES AND LIMITATIONS

CLINICAL LECTURE AT NEW YORK SESSION

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PHILADELPHIA

Only four years has elapsed since the publication by Colebrook and Kenny [1] of the first statistically significant evaluation of sulfonamide therapy in a single disease. They observed a striking reduction in the incidence of invasive complications of postpartum hemolytic streptococcus infections; they witnessed the recovery of patients with widespread peritonitis and septicemia who, except for the drug, would probably have died; they found that no pelvic abscesses occurred in any of the sixty-four patients sick enough to warrant treatment by an experimental drug, while late pelvic abscesses did develop in four of the twenty patients who came in with mild infections which were not treated. These observations were a convincing demonstration of the possibilities of bacterial chemotherapy and were especially convincing to some of us who were fortunate enough to be able to follow some of the cases at Queen Charlotte's Hospital. On the other hand, the limitations of the treatment were also suggested in their study by the failure of the drug to bring about the disappearance of hemolytic streptococci from the lochia of convalescent patients and by the deaths which occurred, in spite of treatment, of patients in whom suppurative thrombophlebitis and acute endocarditis developed.

Since the publication of Colebrook and Kenney, the application of sulfonamide therapy has been widely extended and now includes almost the whole field of surgical infections. A succession of clinical reports have reaffirmed the unquestionable value of chemotherapy in infections due to group A hemolytic streptococci and have added those due to pneumococci, meningococci and gonococci. It seems probable that the use of sulfanilamide in conjunction with surgery will bring about a significant reduction in the mortality of appendical peritonitis.[2] Clinical trial of various compounds of the sulfonamide group is yielding varied results in staphylococcic infections,[3] chronic ulcerative colitis [4] and lymphopathia venereum;[5] a final evaluation of the effectiveness of chemotherapy in these diseases awaits further study, but in all of them drug treatment will probably occupy a legitimate place.

An important practical question now facing the surgeon is "What can chemotherapy be expected to accomplish in the prevention and treatment of surgical infections, and how may chemotherapy and surgical treatment be rationally employed together to achieve the best results?" It is my purpose in this paper to attempt an answer to this question by interpreting the possibilities and limitations of chemotherapy in lesions of different pathologic types.

THE MODE OF ACTION OF SULFANILAMIDE IN RELATION TO SURGICAL INFECTIONS

An adequate explanation of the mode of action of the sulfonamides in biochemical terms has not yet been supplied. It is reasonable to assume, however, on the basis of a considerable amount of laboratory evidence, that these drugs act in infectious lesions by producing an environment in the body tissues and fluids which is unfavorable for bacterial multiplication. As the capacity of the bacteria to multiply is depressed, their invasiveness is diminished and their vitality reduced to a point at which the natural defenses of the body can dispose of the surviving organisms. However, there are factors which modify this so-called bacteriostatic effect of the drug. Among the most important of these are:

1. The ratio between the number of bacteria and the concentration of the drug in the infected zone.
2. The activity of the antibacterial defense in the area of infection.
3. The amount of proteolysis of tissue accompanying the inflammatory process; its content of substances likely to antagonize sulfonamide bacteriostasis.

Of course each of these factors may vary independently of the others during the course of the infection. The net chemotherapeutic response will be a resultant of the integration of these several variables. For example, in an area of cellulitis a certain concentration of the drug may induce bacteriostasis at the periphery of the lesion, owing to a favorable adjustment of the other modifying factors. At the center of the lesion the same concentration of the drug may have little effect because of local chemical alterations which encourage bacterial survival and antagonize drug bacteriostasis. Thus it appears that the pathologic character of the infectious lesion is of primary importance in determining the effectiveness of sulfanilamide; the particular bacterial species involved assumes a parallel but secondary importance because its varying activity as a parasite induces tissue lesions of different pathologic character and of different chemical environment for bacterial metabolism.[6]

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From the Surgical Service of the Hospital of the University of Pennsylvania and the Harrison Department of Surgical Research of the University of Pennsylvania School of Medicine.

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5. Hebb, Arthur; Sullivan, S. G., and Felton, L. D.: The Treatment of Lymphopathia Venereum with Sodium Sulfanilyl Sulfanilate and Sodium Sulfanilate, J. Med. **21**: 5 (March) 1940.

6. Lockwood, J. S.; Coburn, A. F., and Stokinger, H. E.: Studies on the Mechanism of the Action of Sulfanilamide: I. The Bearing of the Character of the Lesion on the Effectiveness of the Drug, J. A. M. A. **111**: 2259 (Dec. 17) 1938.

THE RELATIONSHIP BETWEEN THE PATHOLOGIC CHARACTER OF THE LESION AND THE EFFECTIVENESS OF CHEMOTHERAPY

As experience with bacterial chemotherapy has accumulated during the past few years there has been a tendency on the part of most writers to think solely in terms of bacteriologic specificity in predicting or interpreting chemotherapeutic effects. Experimental results clearly show that different bacteria vary in their general susceptibility to the bacteriostatic effects of compounds of the sulfonamide group. However, in evaluating chemotherapeutic effects in animal infections and in man it is advisable to keep in mind that from a practical standpoint the pathologic characteristics of the lesion under treatment are also of great importance. Diffuse infections characterized by the rapid multiplication and dissemination of invasive bacteria in tissues of relatively normal architecture or in fluids closely resembling normal serum or lymph are likely to respond favorably to chemotherapy. This group includes, specifically, the early stages of cellulitis, lymphangitis, erysipelas and lobar pneumonia and probably also acute pyelonephritis and infections of the cerebrospinal fluid. Whether the causative organism is a hemolytic streptococcus, a staphylococcus or a pneumococcus makes some difference in the choice of a drug, perhaps, but these lesions are generally susceptible regardless of the bacterial species. Sulfapyridine, which is apparently a more polyvalent drug than sulfanilamide, will be effective in the great majority of infections of this pathologic type, and the bacteriologic aspects are of secondary importance.

Infections of serous and synovial membranes such as peritonitis, pleuritis and suppurative arthritis (at least in their early stages) constitute another broad group of lesions which are generally susceptible to sulfonamide therapy. Diffuse non-necrotizing peritonitis in animals and in man is likely to respond to treatment whether the organism is a hemolytic streptococcus,[7] a pneumococcus,[8] a colon bacillus [2] or even a Welch bacillus.[9] Pleural effusions which commonly develop during lobar pneumonia rarely progress to the formation of empyema in patients who have been treated with chemotherapeutic substances. Flippin and our group at the University of Pennsylvania treated 160 patients with type I pneumonia during 1938 and 1939, and the incidence of empyema was only 1.9 per cent in contrast with the "prechemotherapeutic" incidence of 13 per cent reported by Reimann for this type.[10] I have seen several cases in which clinical and laboratory evidence of acute suppurative arthritis developed during the course of a septic infection and in which the arthritis subsided under chemotherapy without the necessity for surgical drainage. Infections of serous and synovial cavities have certain definite pathologic features in common, the most important probably being the early mobilization of an abundant protective mononuclear cell reaction, which Gay [11] has shown is a highly effective mechanism in killing bacteria. This cellular response is given added time to become mobilized when a substance like sulfanilamide is present to hold down the multiplication and toxin production of the infecting organisms. Furthermore, the lining membrane has a good blood supply and is resistant to the necrotizing action of proteolytic enzymes liberated during inflammation by leukocytes and bacteria. It has been shown that one of the most important factors conditioning the magnitude of sulfanilamide action is the amount of products of tissue or bacterial proteolysis in the environment. The capacity of endothelial surfaces to resist proteolysis is therefore another probable reason for the effectiveness of sulfonamide therapy in these infections.

So far I have considered the pathologic types of infectious lesions which are generally susceptible to sulfonamide therapy. It will be noted that they are all early lesions in which treatment by surgical methods has been more often harmful than beneficial. There are, on the other hand, certain definite types of lesions which are quite resistant to chemical treatment. The most conspicuous in this group are the localized abscesses of soft tissue or bone. Bacteriologic specificity again has only a limited significance in the chemotherapy of localized necrotic lesions in soft tissue, bone, pleura or peritoneum. They all tend to be resistant, regardless of the type of organism present. Use of the appropriate drug may have some effect in preventing spread of the infection to adjacent tissues and may actually mask the clinical signs and symptoms of the abscess. Prolonged treatment for a month or two may sometimes allow sterilization of the abscess, but as a general rule such a course will be unpractical and inadvisable. Premature withdrawal of the drug is likely to be followed by reactivation of the infection.

Suppurative thrombophlebitis is another type of pathologic lesion which is comparatively resistant to chemotherapy. The causative organism may be Streptococcus haemolyticus, Streptococcus viridans or Staphylococcus aureus. Chemotherapy will cause blood cultures to become sterile in a case of septicemia or spinal fluid cultures to become sterile in a case of meningitis, but the existence or development of a suppurative thrombophlebitis will make reinfection probable and will in any event greatly prolong the period of recovery.[6]

The practical significance of the emphasis which has been placed here on the pathologic characteristics of surgical infections is that it indicates the place of surgery in the present day treatment of infections. At some time during the clinical course of almost any surgical infection there is likely to develop a pathologic lesion which will not be susceptible to chemotherapy. When this lesion is dealt with surgically, at the right time, the course of treatment can be shortened (which is highly advantageous in preventing toxic reactions) and the chances of final recovery may be considerably increased. The process requiring surgical attack may be an abscess at the primary site of infection or in a lymph node draining the area. It may be a focus in a long bone or in a mastoid. Furthermore, the surgeon who recognizes the limitations of chemotherapy will not be tempted to employ any drug as a substitute for surgery in a necrotizing process such as acute appendicitis. He will limit the application of chemotherapy in this condition to the postoperative treatment of peritoneal infection beyond the limits of the appendix.[2]

The limitations of sulfonamide therapy in terms of pathology are well illustrated in the staphylococcic infections. One may as readily account for the relative resistance of staphylococcic infections on the basis of

7. Lockwood, Coburn and Stokinger.[6] Ladd, Botsford and Curnen.[8]

8. Ladd, W. E.; Botsford, T. W., and Curnen, E. C.: Primary Peritonitis in Infants and Children: A More Effective Treatment, J. A. M. A. **113**: 1455 (Oct. 14) 1939.

9. Bliss, Eleanor A.; Feinstone, W. H.; Garrett, Alice W., and Long, P. H.: Sulfapyridine and Sulfanilamide in Experimental Pneumococcal, Meningococcal, Welch Bacillary, and Friedländer's Bacillary Infections in Mice, Proc. Soc. Exper. Biol. & Med. **40**: 619 (April) 1939.

10. Reimann, H. A.: The Pneumonias, Philadelphia, W. B. Saunders Company, 1938.

11. Gay, F. P.: Agents of Diseases and Host Resistance, Springfield, Ill., Charles C. Thomas, Publisher, 1935, p. 306.

their pathologic characteristics as on the basis of the comparative resistance to sulfonamide bacteriostasis which the staphylococcus possesses. The conspicuous features of staphylococcic infection are tissue necrosis, suppurative phlebitis and the early tendency to form suppurative metastatic lesions. As a general rule the recovery of patients with staphylococcic septicemia, even with treatment by a drug having a high experimental antistaphylococcic effect, will probably depend on whether the primary distributing focus can be detected and drained. It is doubtful whether the specificity of any new compound in the sulfonamide group will be sufficient to overcome the protective "antibacteriostatic" environment which the staphylococcus provides for itself in localized lesions.

Surgical treatment has not by any means been supplanted by sulfonamide therapy. On the surgeon still rests the responsibility for first detecting and then draining or removing the localized suppurative distributing foci which chemotherapy cannot successfully attack. The presence of one of the sulfonamide compounds in the tissue fluids of the potentially septic patient will help to protect him against the consequences of dissemination produced by whatever surgical procedure is necessary in eradicating the distributing focus. The masking of some of the diagnostic signs of infection by sulfonamide treatment appears to render the detection of obscure foci even more difficult than formerly, and new improvements in diagnostic technic may have to be developed. The sulfonamides are really effective principally against the invasive manifestations of infection which surgical treatment has in the past been more likely to aggravate than to cure.

In summary, it might be said that a lesion which is characterized by minimal loss of tissue architecture, and an exudate which is "serous," composed chiefly of lymph, bacteria and inflammatory cells, is likely to respond very rapidly to sulfonamide therapy. On the other hand, when the exudate is thick and purulent, having a high content of products of tissue proteolysis and many dead bacteria and phagocytes, the response to chemotherapy will be relatively slight except at the periphery, where bacteria are lodged in tissues which have not yet become broken down. Sulfanilamide will attack the invasive component of bacterial infections, but the localized abscess and the necrotic distributing focus are problems for surgical drainage or excision. In these areas the bacteria remain potentially invasive; if the inhibitory effect of the drug is removed and host resistance is still inadequate, reinvasion occurs.

GAS GANGRENE

Experimental results with sulfanilamide treatment of Clostridium welchii infections in small animals have not been encouraging. Long and Bliss [9] and Stephenson [12] have shown that mice may be protected against lethal doses of the organisms administered intraperitoneally. However, the Welch bacillus produces its toxin in the presence of devitalized muscle tissue, and the invasive disease produced by intraperitoneal infection of mice is not at all comparable to the lesion of gas gangrene as it occurs clinically. When the bacteria are introduced intramuscularly, even after having been washed free from preformed toxin, the results have been uniformly negative. Erb [13] in our laboratory could find no protection of pigeons with sulfanilamide given before and after infection, in contrast to antitoxin, which was highly effective. Kendrick [14] obtained similar results with guinea pigs, and Stephenson was unable to protect mice which had been infected intramuscularly. Bohlman's [15] early report of recovery in three cases in which a clinical diagnosis of gas gangrene was made scarcely constitutes adequate proof of the specific value of the drug against Clostridium. For the present it would seem that our chief reliance should be on prevention of gas gangrene by débridement of susceptible wounds and administration of prophylactic antitoxin. It is possible that sulfanilamide treatment might have some value in limiting the activity of pyogenic cocci, which are known frequently to prepare the ground for gas gangrene. One would therefore be justified in using one of the sulfonamide preparations in conjunction with other measures, while recognizing the fact that the drug perhaps has little effect on Clostridium itself.

THE PROPHYLACTIC USE OF SULFANILAMIDE

If pathogenic bacteria are implanted in a fresh wound they will, after a few hours, start to multiply, utilizing the tissue fluids in the wound as a culture medium. If there are foreign bodies or devitalized tissues in the wound, the environment becomes rapidly favorable for bacterial growth and toxin production.

Prior to the introduction of the sulfonamides it was recognized that the most important consideration in preventing wound infections was to employ gentle handling of tissues in operative procedures and to carry out thorough débridement and cleansing of grossly contaminated accidental wounds before bacteria had had time to start to multiply actively. The prophylactic use of the sulfonamide compounds in prevention of wound infection is a supplementary means of holding down the multiplication of bacteria which gain access to an operative wound or cannot be removed by débridement from a traumatic wound. Sulfanilamide action is maximal when the number of bacteria is small, the amount of devitalized tissue slight and the concentration of the drug high. Under these conditions there may occur restriction of the outgrowth of types of bacteria which are usually quite resistant to the bacteriostatic effects of the drug. If an effective concentration of the drug can be added to the tissue fluids of the wound before multiplication has actually commenced, the normal tissue defenses will have an opportunity to become mobilized.

The principle of prophylactic treatment is now being applied by the British Royal Army Medical Corps in the management of war wounds.[16] It was reported in an official study [17] that 70 per cent of fatal infections during the last war were due to hemolytic streptococci. It may be that in the current war the incidence of such infections can be greatly reduced. At the Hospital of the University of Pennsylvania we have for three years been using sulfanilamide by mouth in the prophylactic treatment of severe compound fractures. Infection has probably been prevented in some of these cases. Prophylactic sulfanilamide is now being used also in industrial practice in an effort to reduce the amount and duration of disability from infection following injuries

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16. Royal Army Medical Corps Memorandum, Lancet **2**: 996 (Nov. 4) 1939. Fuller, A. T., and James, G. C.: Dosage of Sulfanilamide in Prophylaxis of Wound Infections, ibid. **1**: 487 (March 16) 1940.
17. Douglas, S. R.; Fleming, A., and Colebrook, Leonard: Studies in Wound Infections, Medical Research Council, Special Report Series No. 57, London, His Majesty's Stationery Office, 1920.

in shops and factories.[18] While the theoretical value of such treatment cannot be contested, there are some real dangers to be considered from its indiscriminate application in all types of trivial injuries. Apart from the fact that toxic effects appear to occur more frequently and with greater severity in ambulatory individuals, there is the added danger that the drug will produce motor incoordination and other effects in the central nervous system. No person should be allowed to operate a machine of any sort while taking sulfanilamide. Therefore it would seem advisable to restrict the prophylactic use of sulfanilamide to patients whose injuries are sufficiently disabling to demand their complete inactivity.

Jensen, Johnsrud and Nelson[19] have carried out a clinical and experimental study of the effect of implanting crystalline sulfanilamide into freshly debrided compound fracture wounds. When from 5 to 10 Gm. of crystals is placed in the wound before closure the drug concentration in the wound remains above 200 mg. per hundred cubic centimeters for more than thirty hours. Such a concentration would be highly effective in inhibiting the growth of even resistant organisms such as Staphylococcus aureus or Clostridium during a critical stage of wound repair. There was no evidence that the drug interfered in any way with wound healing. In their series, thirty-nine drug treated compound fractures healed without infection, while infection occurred in 27 per cent of ninety-four fractures treated by similar methods but without sulfanilamide. A distinct hazard in this application of sulfanilamide, particularly if amounts as high as from 15 to 20 Gm. are used, is the possibility of severe toxic reactions in hypersensitive persons. While it is unlikely that this danger would be sufficiently great to contraindicate the method if it were the only possible means of controlling infections in compound fractures, it will be important to find out whether local implantation gives better results in practice than oral dosage. Clinical studies now in progress may justify the use of crystalline drug implanted locally in the prevention of infection in other types of surgical wounds, including large hernias, lobectomies and pneumonectomies, and contaminated intestinal resections. But for the present it seems to me that local implantation of the drug should be used only to supplement oral administration and not in place of it.

THE PRACTICAL APPLICATION OF SULFONAMIDE THERAPY IN SURGICAL INFECTIONS

This section is an attempt to set down, within the limits of a brief review, some notes on chemotherapy as applied to types of infections commonly encountered in general surgical practice. The suggestions put forward are altogether tentative and subject to modification with new developments in this rapidly changing field.

General Considerations. — 1. Choice of Drugs: Sulfanilamide appears still to be the drug of choice in hemolytic streptococcus infections and in nonspecific prophylaxis because:

(*a*) The incidence of serious toxic complications is relatively low and patients are not usually nauseated by it.

(*b*) By altering dose schedules it can be employed to provide high blood concentrations for a short period or low blood concentrations for a long period.

(*c*) It can be administered subcutaneously in 0.8 per cent solution in physiologic solution of sodium chloride when oral administration is inadvisable and can be implanted locally without irritation.

In pneumococcic infections sulfapyridine and sulfathiazole are more effective than sulfanilamide. Of these two the latter is perhaps preferable because it is less likely to produce nausea and vomiting.

In staphylococcic infections the value of sulfanilamide is quite limited, partly because of the pathologic characteristics of infections due to this organism. While sulfathiazole and sulfamethylthiazole appear to be more highly bacteriostatic for staphylococci than sulfanilamide, the relative clinical value of these drugs has not yet been determined.

2. Dosage and Methods of Administration: The daily dose is divided into six fractions when given by mouth and four fractions when given parenterally. The amount administered varies with the severity and relative susceptibility of the lesion under treatment. It is usually from 6 to 10 Gm. the first day, from 5 to 7 Gm. the second day and from 4 to 6 Gm. the succeeding three days. If a clinical response is obtained within forty-eight hours and the lesion is one in which relapse appears to be unlikely, the treatment is stopped on the fifth day. If the response to treatment is slow, but nevertheless apparent within two days, the treatment may be continued for from six to ten days. If the lesion is a chronic one and prolonged treatment of more than two weeks appears desirable, the daily dose is usually from 2 to 4 Gm. For treatment of this type it might be desirable to use a compound such as azosulfamide or benzylsulfanilamide,[20] which liberates free sulfanilamide more slowly.

On rare occasions one is confronted with a patient displaying some of the signs of invasive infection but in whom a definite diagnosis cannot be made. In such cases a "therapeutic test" with one of the sulfonamides may appear to be indicated. If no evidence of a therapeutic response is obtained within forty-eight hours it is probable that further continuation of the drug will be futile and perhaps undesirable. The same rule probably should be applied in the treatment of invasive infections due to bacteria whose susceptibility to chemotherapy has not yet been determined.

Sulfanilamide is usually given by mouth. Solutions for parenteral use are prepared by adding 8 Gm. of crystalline sulfanilamide to a liter of hot physiologic solution of sodium chloride, which is then allowed to cool.

NOTES ON CHEMOTHERAPY IN THE PREVENTION AND TREATMENT OF SPECIFIC LESIONS ENCOUNTERED IN GENERAL SURGICAL PRACTICE

Diffuse Cellulitis and Lymphangitis.—Prophylaxis: Administration of sulfanilamide by mouth for five days is probably of value in severely traumatized, contaminated wounds and compound fractures, but only in conjunction with, and not as a substitute for, thorough débridement and cleansing of the wound. Local implantation of sulfanilamide crystals in compound fracture wounds has been reported to be very effective.[19]

Treatment: Sulfanilamide in full doses should be used for the first forty-eight hours, followed by gradually diminishing doses until the seventh day. The management thereafter will depend on whether or not

18. Brylski, F. J.: Prontylin and Neoprontosil: Their Use in Industry, Indust. Med. **8**: 469 (Nov.) 1939.

19. Jensen, N. K.; Johnsrud, L. W., and Nelson, M. C.: Local Implantation of Sulfanilamide in Compound Fractures, Surgery **6**: 1 (July) 1939.

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localized abscess formation has occurred. Immobilization, elevation and heat should be used in conjunction with chemotherapy.

Acute Lymphadenitis.—Prophylaxis: Prophylactic treatment consists of the early treatment of cellulitis and lymphangitis.

Treatment: When suppuration is doubtful, sulfanilamide is given until fever and local signs of acute inflammation subside, usually for from seven to ten days. Complete resolution will not occur if pus is present. When suppuration is definite, sulfanilamide may be given for one or two days, after which the abscess should be incised and drained. Chemotherapy may then be continued for a few days, depending on whether there is any residual peripheral cellulitis.

Soft Tissue Abscess.—Prophylaxis: Early treatment of cellulitis may prevent abscess formation.

Treatment: Surgical drainage is indicated. Chemotherapy should be used only if cellulitis also is present.

Nonsuppurative Phlebitis.—Chemotherapy is of little value. Good results are being obtained from bandaging the affected extremity and from paravertebral sympathetic block.[21]

Suppurative Thrombophlebitis. — Prophylaxis: The avoidance of continuous venoclysis in septic patients is probably desirable.

Treatment: Chemotherapy is of limited value in attacking the local lesion but should be used in full doses in order to limit dissemination. Heparin may be of value in limiting propagation of the thrombus. Ligation of the vein proximal to the area of infection may be helpful in special cases.

Septicemia. — Prophylaxis: Chemotherapy and immobilization should be applied to early lesions likely to lead to septicemia. Surgical procedures should be avoided in diffuse cellulitis, but if unavoidable (as in acute tenosynovitis) the use of sulfanilamide before and after operation may help to minimize dissemination.

Treatment: Chemotherapy is indicated in full doses. If the drug is effective, marked clinical improvement is usually evident within forty-eight hours. The prognosis is much better if foci of distribution or localization can be drained. Frequent small (250 cc.) transfusions of fresh whole blood are probably helpful. Intravenous "double potency" bacteriophage[22] is promising in staphylococcic septicemia, particularly in conjunction with chemotherapy.

Osteomyelitis.—Sulfonamide therapy may be directed against the dissemination of the infection but is probably of only limited value in the treatment of established bone foci. It should be used during and for a few days after surgical procedures likely to cause dissemination.

Pulmonary Abscess.—Chemotherapy is apparently of little or no value because the organisms are drug resistant and the lesions are characterized by extensive necrosis.

Infections of Serous or Synovial Cavities.—Chemotherapy is particularly successful in the prevention and treatment of infections of serous and synovial cavities. This is probably because of the highly developed local cellular defense, the resistance to necrosis of the lining membrane and the readiness with which adequate concentrations of the drug occur in the fluids.

Pleuritis and Empyema. — Prophylaxis: Chemotherapy might be of value if used before and after pneumonectomy or lobectomy. Chemotherapy of pneumonia tends to prevent empyema.

Treatment: Chemotherapy and drainage by aspiration may be used if the exudate is serous. Resolution without the necessity for open drainage is likely under these conditions. Rib resection and drainage will be required as soon as the exudate is frankly purulent. Sulfonamide therapy in small doses after operation may shorten the period of drainage.

Primary Peritonitis. — Chemotherapy should be started in full dosage after the diagnosis has been established by paracentesis or by exploratory laparotomy through an incision of minimal size.[7] Appendectomy should be avoided in these cases. The choice of drug will depend on the organism found. Other treatment directed against dehydration, distention, hypoproteinemia and electrolyte imbalance is of great importance.

Peritonitis Secondary to Inflammation or Perforation of the Bowel.[23]—Prophylaxis: Sulfanilamide therapy has been recommended for one day before and for four days after intestinal resections.[24]

Treatment: Sulfanilamide treatment appears to be of value in all cases of acute appendicitis which, at operation, show evidence of infection beyond the limits of the appendix itself. Appendectomy is essential. Chemotherapy may be instituted also in cases of peritonitis secondary to soiling of the peritoneum from other causes but only to supplement surgical and other therapeutic procedures of established value. In cases of peritonitis the drug is given parenterally until oral feedings are permissible.

Acute Suppurative Arthritis.—Chemotherapy should be started as soon as the diagnosis has been made, either on clinical grounds or by aspiration and study of the exudate. If drug therapy is started early in the disease the results are very good and surgical open drainage will probably not be necessary. (The treatment of rheumatic fever or rheumatoid arthritis with sulfonamide is contraindicated.[25] Treatment should be continued for about a week after all clinical signs of inflammation have subsided.

Meningitis. — Prophylaxis: Prophylactic treatment consists of sulfonamide treatment of otitis media, mastoiditis and invasive sinusitis, in combination with appropriate surgical measures. Chemotherapy alone will not insure against a late spread of infection to the meninges from a suppurative focus in bone or blood vessels but will sometimes mask the existence of such a focus.

Treatment: Chemotherapy should be instituted in full doses by mouth or parenterally. Some authorities recommend administration of the drug intrathecally as well.[26] The use of a drug having specific bacteriostatic effect on the causative organism may bring about marked clinical improvement and clearing of the spinal fluid, but relapse is very likely to occur unless the focus that feeds the spinal fluid can be drained or removed. Treatment should be continued in gradually diminishing doses for at least two weeks after apparent clinical

21. Ochsner, Alton, and DeBakey, Michael: Thrombophlebitis: The Role of Vasospasm in the Production of the Clinical Manifestations, J. A. M. A. **114:** 117 (Jan. 13) 1940.

22. Longacre, A. B.; Jern, H. Z., and Meleney, F. L.: The Treatment of Staphylococcic Septicemia with Bacteriophage, Surg., Gynec. & Obst. **70:** 1 (Jan.) 1940.

23. Lockwood, J. S., and Ravdin, I. S., to be published. Ravdin, Rhoads and Lockwood.[2]

24. Lockwood, J. S., and Rhoads, J. E.: The Use of Sulfanilamide in the Treatment of Peritonitis, S. Clin. North America **19:** 1457 (Dec.) 1939.

25. Swift, H. F.; Moen, J. K., and Hirst, G. K.: The Action of Sulfanilamide in Rheumatic Fever, J. A. M. A. **110:** 426 (Feb. 5) 1938.

26. Neal, Josephine B.: The Treatment of Acute Infections of the Central Nervous System with Sulfanilamide, J. A. M. A. **111:** 1353 (Oct. 8) 1938.

recovery. Most of the cures in meningitis due to hemolytic streptococci, pneumococci and staphylococci are a result of skilful and timely surgery in conjunction with chemotherapy and are not by any means due to the drug alone.

CONCLUSIONS

1. The pathologic character of the infectious lesion is an important factor in determining the effectiveness of sulfonamide therapy.

2. Surgical treatment is required in eradicating localized suppurative foci which are resistant to chemotherapy.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

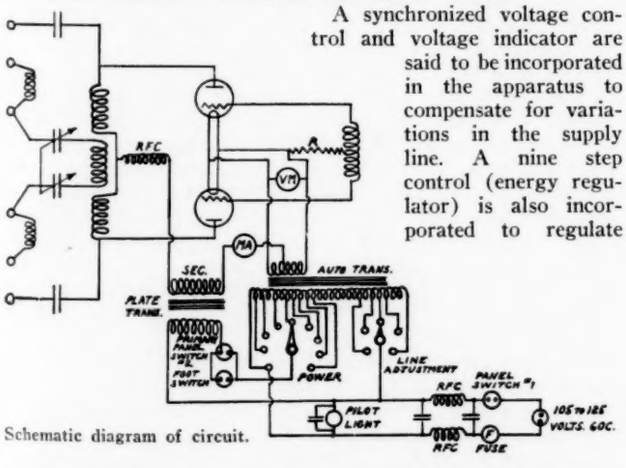
CONTINENTAL SHORT WAVE UNIT MODEL SW-200 ACCEPTABLE

Distributor: Bedford Surgical Company, Inc., 1326 Fulton Street, Brooklyn.

The Continental Short Wave Unit, Model SW-200, is used for medical and surgical diathermy. Pads, cuffs, inductance coil, surgical accessories and metal electrodes are supplied as standard equipment. The shipping weight of the unit is 175 pounds.

Continental Short Wave Unit, Model SW-200.

The firm states that the unit operates on approximately 12 meters and utilizes two tubes in a self-rectifying, push-pull tuned plate, tuned grid oscillating circuit. The tubes consist of two HF-120 oscillator tubes. The patient's circuit is inductively and capacitatively coupled to the oscillating circuit and is controlled by two variable condensers in series connected to both sides of the patient's outlets, coupled to a single control. In tests performed by the Council the power input was found to be 800 watts and the output 300 watts; transformer temperature was 78.2 C. after the unit had been operated at full load for two hours. This temperature comes within the limits of safety prescribed by the Council.



Schematic diagram of circuit.

A synchronized voltage control and voltage indicator are said to be incorporated in the apparatus to compensate for variations in the supply line. A nine step control (energy regulator) is also incorporated to regulate energy to the patient's circuit. Three radio frequency chokes in the circuit are said to reduce radio interference.

Data concerning deep muscle temperature measurements was submitted by the firm and confirmed by the Council. The data are as follows:

DEEP MUSCLE TEMPERATURE MEASUREMENTS

DOUBLE CUFFS

Technic: Double cuffs were placed 7 inches center to center, each equidistant from the thigh cannula. The cuffs were 2¼ by 19 inches, and three-fourths inch of felt was used for spacing. The current on the ammeter was 200 milliamperes plate circuit.

Average temperature of six tests: Deep muscle, initial 97.4, final 106.7. Oral, initial 98.4, final 98.6.

CABLE

Technic: Four turns of cable were placed 8 inches center to center equidistant from the thigh cannula with three-fourths inch felt and towel spacing. The plate reading was 200 milliamperes.

The average temperatures of six tests were: Deep muscle, initial 97.8 F., final 106.8 F. Oral, initial 98.3 F., final 98.6 F.

The Council report indicated that the Continental Short Wave Unit, Model SW-200, had been used almost daily on about fifteen different patients. It was found that the heat is just as effective as that of other short wave apparatus.

Clinical investigation of the unit by the Council revealed that spacers might well be used with the coil because of its marked flexibility and small diameter. The apparatus is easily adjusted and applied.

The Council voted to accept the Continental Short Wave Unit, Model SW-200 for inclusion on the Council's list of accepted devices.

B-L-B INHALATION APPARATUS ACCEPTABLE

Manufacturer: The Ohio Chemical & Manufacturing Company, 1177-1199 Marquette Street N.E., Cleveland.

The B-L-B Inhalation Apparatus with Helium-Oxygen Equipment is named for its designers, Boothby, Lovelace and Bulbulian. According to the firm, the advantages of the apparatus are a low purchase and maintenance cost, the efficient use of therapeutic gases, the ability to give therapeutically the desired concentration of oxygen between that in air and pure oxygen, the ability to administer efficiently helium-oxygen mixtures, the mechanical simplicity and ease of operation, and the portability of the apparatus.

The equipment supplied by the firm consists mainly of three parts, the B-L-B Inhalation Apparatus, a reducing regulator and flowmeter for pure oxygen, and a reducing regulator and flowmeter for helium-oxygen mixtures.

The inhalation apparatus is composed of the mask proper and a metal connecting and regulating device which joins the mask to a rubber reservoir rebreathing bag. Two types of interchangeable masks are available. The nasal type leaves the mouth free for talking, eating or drinking, which is an advantage in prolonged use. The oronasal type covers the nose and mouth and is for use by persons who have nasal obstructions or who are mouth breathers. In both types provision is made so that a suction tube can be passed through when it is desired to administer 100 per cent oxygen in combination with the use of the Wangensteen or Miller-Abbott suction method of intestinal decompression. The masks are available in two sizes.

B-L-B Inhalation Apparatus.

By the adjustment of three small portholes in the connecting and regulating device, it is possible to regulate the proportion of atmospheric air admitted to the apparatus which, in conjunction with the appropriate flow of oxygen or helium-oxygen mixtures, gives the desired mixture of the inspired gases.

In use, the compressed oxygen or helium-oxygen mixtures first pass through a reducing valve and flowmeter; next they enter the inlet tube of the B-L-B apparatus and are delivered through a tube to the lower end of the reservoir rebreathing bag. Then they pass into the nose chamber, through the connecting and regulating device, and are inhaled by the wearer. The exhaled gases pass down through the tubes and the connecting and regulating device, where a part of the gases pass out through

any holes that may be open in the rotary sleeve. The remaining portion passes downward into the bag, where it is mixed with the incoming gases.

When the bag becomes distended with the mixture of expired air and incoming gas, the slight pressure then produced permits the excess to escape through the expiratory valve. The expired air thus escaping will be from the latter part of the expiration and will contain the most carbon dioxide and least oxygen. That part of the expired air which passes into the bag first and contains the least carbon dioxide and the most oxygen is available for rebreathing. On the next inhalation the mixed oxygen and expired gases, further admixed with atmospheric air entering through the portholes, are again drawn in.

The Council investigated and used the apparatus clinically and found no objectionable features referable to its construction or to the claims made. Actual gas analyses bore out the stated claims as to efficiency. In patients for whom its use was undesirable, the fault was with the apparatus rather than with the method.

The Council on Physical Therapy voted to accept the B-L-B Inhalation Apparatus with Helium-Oxygen Equipment for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

PRELIMINARY REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING PRELIMINARY REPORT, CONSIDERATION OF COBRA VENOM BEING POSTPONED BY THE COUNCIL TO AWAIT FURTHER EVIDENCE CONCERNING ITS USEFULNESS AND HARMLESSNESS. THE COUNCIL HAS LIKEWISE POSTPONED CONSIDERATION OF THE BRAND SUBMITTED BY THE FIRM OF HYNSON, WESTCOTT & DUNNING UNDER THE NAME COBRA VENOM SOLUTION (SECRETION OF NAJA) AND DESIRES TO EXPRESS ITS APPRECIATION OF THE COOPERATIVE SPIRIT WITH WHICH THE FIRM AIDED THE COUNCIL'S CONSIDERATION. PAUL NICHOLAS LEECH, Secretary.

COBRA VENOM SOLUTION (SECRETION OF NAJA) (HYNSON, WESTCOTT & DUNNING)

Hynson, Westcott and Dunning, Inc., presented for the Council's consideration Cobra Venom Solution (Secretion of Naja). The preparation is proposed for intramuscular injection as a slowly but persistently acting analgesic which lacks the chief disadvantages of morphine. When this report was prepared it was marketed in ampules of 1 cc., each of which represents 5 mouse units. A mouse unit is that amount of cobra venom solution which causes the death of a mouse of average weight of 24 Gm. in twenty-four hours.

The use of venoms or extracts of venomous reptiles as analgesics began about ten years ago when Monaelesser of New York learned that a Cuban leper who had been bitten by a tarantula experienced amelioration of painful and nervous symptoms. In Paris he gave cobra venom to 112 cancer patients in a dilution of 1:80,000 and noticed lessening of pain after four or five doses. Slower development, and even regression, of the tumors was reported at the same time. Since then the use of cobra venom for the relief of pain has been the subject of many investigations.

Nearly all the venoms derived from serpents for therapeutic use contain hemolysin, hemorrhagin, proteolysin and neurotoxin in widely different concentrations and ratios in different species and even in specimens from the same serpent under varying conditions. Cobra venom contains far greater amounts of neurotoxin than that of either the rattlesnake or the moccasin and on this basis rests its use as an analgesic. Chemically it contains the elements carbon, hydrogen, sulfur, oxygen, nitrogen and phosphorus. The dried venom yields 87.56 per cent of protein with the following fractions: globulin 20.31 per cent, albumin 39.69 per cent, primary proteose 11.31 per cent and secondary proteose 16.81 per cent. Lecithin (partly free) and cholesterol may also be found. The toxicity of the venom is attributed to the secondary proteose. Three enzymes have been demonstrated, a proteolytic one which is capable of digesting gelatin, casein, fibrin and crystallized egg albumin; a rennetic enzyme, and one which may split lecithin. The hemolytic power of cobra venom is associated with a fraction composed of globulin and primary proteose.

The effect of cobra venom in the mammalian vascular systems varies with the species. Intravenous injection of the venom into cats anesthetized with dial causes a steep fall in blood pressure, the action being said to be due to obstruction in the pulmonary circulation without contributory heart failure. Injection into the femoral artery causes vasoconstriction of the limb. With survival there is recovery of the blood pressure followed by a slow secondary fall due to loss of circulating fluid, with hemorrhagic edema of the lungs and, in some cases, from heart failure. The effects in cats are different from those in dogs, the fall in blood pressure in the latter being due to vasodilatation rather than pulmonary obstruction, and permeability of the capillaries with loss of fluid causes an increase in the concentration of the hemoglobin. The fall in blood pressure in the dog induced by the intravenous injection of cobra venom is due to a peripheral action similar to that of peptone. Respiration is accelerated slightly by small doses but is decreased with large doses by paralysis of the phrenic nerve. Injection into the veins or lymphatics induces an action similar to that of curare. It has been reported that cobra venom causes the blood sugar to be increased in guinea pigs but has little effect in this respect in the rabbit.

Tissue activity has also been shown to be influenced by cobra venom. Low concentrations of the venom stimulate tissue growth in vitro, whereas high concentrations exert an inhibitive action. These effects are attributed to different types of enzyme action on fibrin. Changes in surface tension opposite in direction to those in viscosity are induced by injection of the venom, probably because of increase in the protein concentration in the plasma. In monkeys it has been shown that the alterations in the reaction of the plasma and the buffering are parallel, the result of carbon dioxide tension caused by the action of the venom on the respiratory center. Venoms and the avenoms of the cobra and vipers retard or cause to regress the growth of the Rous sarcoma in fowls, but the action is not specific. A certain inhibitory action is seen in mammals but large doses of the venom have no effect much beyond the point of injection on rapidly growing carcinomas in rats.

Macht and his co-workers have shown that cobra venom (*a*) inhibits the growth of the roots of lupin seedlings, indicating them to be protoplasm poisons, (*b*) suffers a rapid loss in potency when exposed to ultraviolet radiation, (*c*) stimulates and later depresses the ability of a rat to find its way to food in a maze, (*d*) facilitates mathematical calculations in man, (*e*) increases acuity of vision and widens the field for certain colors without affecting the size of the pupil, (*f*) slightly increases acuity of hearing, (*g*) stimulates the respiration and circulation in the cat but fatal doses cause death by paralysis of respiration, (*h*) exerts its analgesic action in the higher centers of the brain or on some lower synapses but not on the periphery, (*i*) is fatal to the cat if 1.35 mg. per kilogram of body weight is given intravenously, and to the frog if 0.01 mg. per 20-22 Gm. of body weight is given intraperitoneally, (*j*) antagonizes the convulsant action of picrotoxin and certain other convulsants that act on the medulla, (*k*) improves neuromuscular coordination and work, (*l*) usually increases the experimental contraction of the index finger, and in long continued large doses does not appear to impair the functions of the liver or of the kidney of the rabbit.

Varying degrees of success have been reported in the use of cobra venom for the relief of pain in cancer. Many agree that relief of the pain is usually obtained, and in some cases apparent regression of the tumors have been observed. However, the latter effect is doubtful. The types of cancer cases experimented with included cancer of the prostate, bronchus, stomach, lungs, colon and breast. Other diseases causing pain which were reported to be successfully relieved by venom therapy include trigeminal neuralgia, leprosy of the nerve type, rheumatoid arthritis and other forms of arthritis. However, cobra venom seems to be of little value where pressure on a nerve exists. Improvement of appetite, whether a direct effect or due to decreased use of the morphine which had been necessary in so many cases, has been noted. The use of cobra venom in parkinsonian syndrome has been more recently reported.

No serious complications have been reported following therapeutic injection, although local reactions are not unknown. A few investigators have seen headache, nausea, diarrhea, fever and a pain at the site of injection following the use of Cobra venom. No observable changes have been found in the red blood corpuscles, blood pressure, temperature, pulse rate or blood picture, nor has there been found any pathologic condition such as hemorrhage or infiltration, or effects on respiration or the gastrointestinal tract. Pigmentation, however, has occasionally been noticed, lasting for some weeks.

Apparently there are no true contraindications to the use of cobra venom for the relief of pain, but especial care is necessary with patients who have psychic disturbances or severe diseases of the liver or kidneys. No exacerbation of symptoms in cardiac, hypertensive or diabetic patients has occurred, nor has there been found any abnormality in urinalysis.

The technic of dosage is not simple and the optimum dose must be determined separately for every patient. It does not act uniformly as to degree and time in cases presenting approximately similar involvement. The dose is independent of age, well-being and other factors.

The manufacturer of Cobra venom solution, Hynson, Westcott and Dunning, Inc., submitted several clinical papers with the presentation of its preparation, but the Council does not believe that they afford sufficient evidence of a satisfactory nature on which to base an opinion concerning the therapeutic value of the venom. The directions in the specimen package circulars state that the first dose, 0.5 cc., should be injected intramuscularly, and 1 cc. on each of several successive days until definite relief of pain is noted. It is clear, however, that no fixed dosage after the first is available. The greater number of European observers have been influenced by the procedure of Monaelesser and Taguet, who began with doses of about 2½ mouse units and gradually increased this at intervals of two or three days between injections. Some have attained doses of 20 mouse units or more, others have not exceeded 10 mouse units. The frequency of repetition employed is extremely variable. One must determine the single dose, as well as the frequency of repetition, for each patient so far as possible. Without careful supervision it would seem that the venom may do far more harm than good in many cases.

Ten ampules of the Cobra venom solution in a small box were submitted. These have been kept in the box; hence the conditions have been uniform for these ampules, but they show wide differences in color, and on standing different amounts of precipitate are seen. The firm's attention was called to this lack of uniformity, and the Council was informed that the differences are due to the preservative used. While it may be the cause of the precipitate, it does not explain the variability in amount. The firm wrote that the process of preparation has now been improved, but new specimens have not yet been seen. The firm submitted a list of 155 references, but with the exception of those of Macht and his associates there are only three clinical studies made by Americans and published in the United States of which the Council knows and which are suitable for analysis.

Cobra venom is certainly capable of relieving pain under varying conditions and appears to be of distinct value in giving relief from pain in cancer. It often fails completely, and it seldom, if ever, replaces morphine completely for any considerable time. It often causes pain of widely different degrees, probably owing to differences in composition, but this does not necessarily apply to the venom of Hynson, Westcott and Dunning, Inc. Among the disadvantages of Cobra venom which have been observed by European clinicians and others are pain of injection (intense at times), nausea, vomiting and diarrhea. However, Taguet and others have reported the absence of shock or other general or allergic reactions, though the records of patients treated number hundreds.

In summary, the Council considers purified Cobra venom to be of some value for the relief of pain, especially that of inoperable cancer (its use in the early stages would tend to delay curative measures); it does not displace morphine completely in more than relatively few cases but it is of value in these few; it appears to be of limited value in the treatment of tic douloureux and the various conditions commonly grouped loosely under the names of "rheumatism" and "arthritis"; its therapeutic effects are variable and uncertain in all painful conditions; the disagreeable side actions, including nausea, vomiting, diarrhea and pain of injection—even intense pain at times, mentioned in medical journals—must be brought to the attention of those who use Cobra venom; it must not be recommended for those who are severely ill except those suffering from inoperable malignant tumors or from incurable disease; the optimum dosage (after the first single dose) remains to be determined; the effects are not immediate but may take hours to appear.

In view of the lack of sufficient evidence to warrant inclusion in N. N. R. at this time, the Council postponed consideration of Cobra venom and of the submitted brand and authorized publication of the foregoing preliminary report.

In accordance with the Council's custom, the adopted report was sent to the firm before publication. As a result of some correspondence certain editorial changes were made. The firm also informed the Council of its intention to double the strength of the marketed product from 5 mouse units to 10 mouse units per cubic centimeter without change in price.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

SOLUTION OF POSTERIOR PITUITARY (See New and Nonofficial Remedies, 1940, p. 386).

PITUITARY SOLUTION-U. S. P. (U. S. S. P. Co.).—A brand of solution of posterior pituitary-U. S. P.

Manufactured by U. S. Standard Products Co., Woodworth, Wis.
Ampul Pituitary Solution-U. S. P., 1 cc. (U. S. S. P. Co.).
Ampul Pituitary Solution-U. S. P., ½ cc. (U. S. S. P. Co.).
Vials Pituitary Solution-U. S. P., 10 cc. (U. S. S. P. Co.).
Vials Pituitary Solution-U. S. P., 30 cc. (U. S. S. P. Co.).

SULFANILAMIDE (See New and Nonofficial Remedies, 1940, p. 489).

The following dosage forms have been accepted:

Tablets Sulfanilamide, 5 grains-Wyeth.
Prepared by John Wyeth & Brother, Inc., Philadelphia. No U. S. patent or trademark.

Tablets Sulfanilamide, 7½ grains-Wyeth.
Prepared by John Wyeth & Brother, Inc., Philadelphia. No U. S. patent or trademark.

Tablets Sulfanilamide, 10 grains-Wyeth.
Prepared by John Wyeth & Brother, Inc., Philadelphia. No U. S. patent or trademark.

BISMO-CYMOL (See New and Nonofficial Remedies, 1940, p. 147).

The following dosage forms have been accepted:

Bismo-Cymol, 60 cc. Bottle: Each cubic centimeter contains bismocymol equivalent to 50 mg. of metallic bismuth, dissolved in olive oil.
Bismo-Cymol, 500 cc. Bottle: Each cubic centimeter contains bismocymol equivalent to 50 mg. of metallic bismuth, dissolved in olive oil.

PHENOBARBITAL (See New and Nonofficial Remedies, 1940, p. 134).

The following dosage form has been accepted:

Phenobarbital Tablets, 0.1 Gm. (1½ grains).
Prepared by The Smith-Dorsey Company, Lincoln, Neb.

SULFAPYRIDINE (See New and Nonofficial Remedies, 1940, p. 494).

The following dosage form has been accepted:

Capsules Sulfapyridine, 0.25 Gm. (3¾ grains).
Prepared by Parke, Davis & Company, Detroit. No U. S. patent or trademark.

SOLUTION LIVER EXTRACT CONCENTRATED-LILLY.—Now Solution Liver Extract-Lilly, 2 U. S. P. Units Per CC. (See New and Nonofficial Remedies, 1940, p. 329).

Ampoules Solution Liver Extract-Lilly, 2 U. S. P. Units Per CC., 3.5 CC.: Marketed in packages of four 3.5 cc. rubber stoppered ampules.

SOLUTION LIVER EXTRACT PURIFIED-LILLY.—Now Solution Liver Extract-Lilly, 15 U. S. P. Units Per CC. (See New and Nonofficial Remedies, 1940, p. 330).

Ampoules Solution Liver Extract-Lilly, 15 U. S. P. Units Per CC., 10 CC.: Marketed in 10 cc. rubber stoppered ampules.

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SATURDAY, OCTOBER 5, 1940

PHYSICIANS NEEDED FOR INDUCTION BOARDS

After registrants are accepted by local draft boards they will be sent for physical examination to medical induction boards. About one hundred such boards will be set up throughout the country, about half of them near army posts and stations. Each board will consist of three internists, one general surgeon, one orthopedic surgeon, two ophthalmologists, one otorhinolaryngologist, one neuropsychiatrist, one clinical pathologist and one dentist.

As explained by Colonel Love (pages 1201-1202 of this issue), the specialists to be assigned to such service will probably include civilian specialists as well as reserve officers, who will be on temporary duty. Civilian physicians will be on a per diem basis and will be used as long as their services are required. It has been proposed that they be paid at the base pay of major with allowances for travel and subsistence while on duty. Physicians preferred for this service are those who, on account either of age or of physical infirmities or because of reasons affecting their civil life, cannot go into military camp. It has been tentatively estimated that the time required for this service might approximate twenty to thirty days in the period between October 16 and February 1.

In order to aid the Army Medical Department in securing physicians for this service, the Committee on Medical Preparedness requests physicians who wish to volunteer to write at once to the Committee on Medical Preparedness, 535 North Dearborn Street, Chicago, marking the envelop "Induction Boards."

VITAMINS FOR WAR

England, locked in the struggle of total war and conscious of the importance of maintaining at high levels the strength and courage of its people, has fortified margarine with vitamin A and restored calcium and thiamin hydrochloride (vitamin B_1) to flour.[1] This action was taken on advice from the Medical Research Council and with the recommendation of leaders in nutritional research. Sir John Orr[2] and Dr. J. C. Drummond[3] were largely responsible. In consequence, ill effects from deficiency of calcium compounds and vitamin B_1 will be minimized in England notwithstanding lower rations. Vitamin A will accompany whatever edible fats remain available, and calcium and vitamin B_1 will be supplied as long as any cereal food is left.

The slim margin that exists between man's physiologic requirements for vitamin B_1 and his intake of this vitamin has long been known; also the fact that storage of this vitamin is minimal and that debility quickly follows when men are deprived of it. The diets of half the population of England were found[2] to provide a level of intake of vitamin B_1 less than that which the League of Nations Technical Commission regarded as necessary for adult men in peace time. That level was 300 international units a day. For soldiers, however, for men in factories and on the farms, in war time, for long work and short sleep, a level of 300 international units is certainly not optimal.

The Stiebling report from the United States Department of Agriculture[4] revealed a large proportion of "poor" diets in peaceful America with its bursting granaries and troublesome problems of overproduction. The diets were poor in vitamins A, D and B_1 and in calcium. To some extent they were poor for lack of purchasing power, but to a large extent they were poor because of lack of skill in getting good food values for food expenditures. When white flour and sugar provide 50 per cent of the calories, as is the case in England and America, selection of a diet that can be called good, in the sense that it satisfies more than minimal requirements for vitamin B_1 and calcium, is almost impossible except for an expert.

Recent reports on induced vitamin B_1 deficiency[5] bear directly on the importance of a liberal allowance of vitamin B_1 for a people engaged in war. Restriction of the intake of this vitamin in a group of healthy subjects, otherwise adequately fed, provoked, among other signs and symptoms, moodiness, sluggishness, indifference, fear, and mental and physical fatigue. The states of mind and body observed in these subjects were such as would be least desirable in a population facing invasion, when maintenance of stamina, determination and hope may mean defeat or successful resistance.

Other subjects in the experiment mentioned received thiamin hydrochloride in such an amount that their intake of thiamin would be almost, if not quite, up to the standard set for this vitamin by the League of Nations Technical Commission. These subjects remained in apparent good health for weeks, but when, at the end, more of this vitamin was administered—enough to raise the intake to 600 international units a day—alertness increased and measured capacity for physical work was almost doubled.

1. Moran, T., and Drummond, J. C.: Reinforced White Flour, Nature **146**: 117 (July 27) 1940.

2. Orr, Sir John: Food, Health and Income: Report on a Survey of Adequacy of Diet in Relation to Income, London, Macmillan & Co., 1936 (summary in Lancet **1**: 679 [March 21] 1936).

3. Drummond, J. C.: Margarine, Nature **145**: 53 (July 13) 1940.

4. Stiebling, Hazel K., and Phipard, Esther F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities, U. S. Dept. Agr. circ. 507, 1939. Stiebling, Hazel K.: Dietary Levels in the United States, J. Nutrition **19** (supp.): 21 (June) 1940.

5. Williams, R. D.; Mason, H. L., and Smith, B. F.: Induced Vitamin B_1 Deficiency in Human Subjects, Proc. Staff Meet., Mayo Clin. **14**: 787 (Dec.) 1939. Williams, R. D.; Mason, H. L.; Wilder, R. M., and Smith, B. F.: Observations on Induced Thiamine (Vitamin B_1) Deficiency in Man, Arch. Int. Med., to be published.

This suggests that efficiency for prosecution of a war can be increased by the simple expedient of providing a very little more of vitamin B_1 than the public is receiving. This subject is also receiving consideration by those responsible for our national defense.

USE AND ABUSE OF ADVERTISING BROCHURES

One of our colleagues who apparently has plenty of space at home decided about a year ago to save every piece of advertising literature in the field of therapy that came to him during 1939. A large closet was set aside for the purpose; the latest report indicates that material thus collected weighed over three hundred pounds. Even at the current price paid for waste paper, the collection will not pay for the cost of storage. The fact gives opportunity, however, for some philosophic considerations on the use and abuse of brochures circulated by manufacturers of proprietary products as their contribution to the education of the physician.

As examples of the printing art, many advertising brochures are good. As sources of scientific information in certain fields, some may be valuable. Some of the lithographs and four-color reproductions which illustrate anatomic appearances, physiologic functions and therapeutic technics are superior to anything that can be found in the available textbooks. Yet by no stretch of the imagination can any of these brochures be considered wholly scientific, since their purpose is obviously to sell specific products. Manufacturers are naturally averse to discussing in their brochures competitive products of the same type or alternative technics. They tell a story but seldom or never the whole story.

The manufacturer who reaches the general practitioner first and who accustoms him to the use of certain materials endeavors to retain his patronage for a considerable time. Hence the introduction of such substances as insulin and liver extract, which demand technical knowledge for determination of dosage and method of administration, is associated with the wide distribution by the manufacturers of extensive brochures discussing these matters. The introduction of new serums for use in pneumonia, and of sulfapyridine, has elicited a series of brochures dealing with these products. The newer anesthetics gave rise to theses dealing with the nature and composition of the products, as well as heavily illustrated brochures dealing with the technic of use.

As part of its function, the Council on Pharmacy and Chemistry of the American Medical Association has been accustomed to examine such brochures to make certain that the claims made are in accord with the acceptance of the product by the Council; thus the Council actually gives added prestige to brochures on products which are accepted. The difficulties involved in the examination of such a vast amount of material should be obvious. Indeed, some members of the Council look askance on brochures that seem overelaborate as to production and illustration. It requires great time and effort to evaluate such monographs and to check and verify alleged scientific statements which seem to be more interested in selling than in science.

The whole field of medical publication is undergoing an obvious transformation. The speed of the times would seem to demand more in the nature of monographic publications dealing with a single subject and less of extensive textbooks which tend to become obsolete, at least in portions of their text, in a short time. Development of this trend for the monograph in the field of unbiased scientific literary production would be useful to the medical profession; it might lead to less abuse in the publication and distribution of brochures by commercial interests.

ACETYLSALICYLIC ACID DEATHS

The only country in the world that permitted a patent for acetylsalicylic acid (aspirin) was the United States. The "Bayer" patent expired in 1917; since then the supply of acetylsalicylic acid or aspirin on the American market has been essentially of the same quality, irrespective of the manufacturer. Even after the expiration of the patent in 1917 it has paid the Bayer Company to continue the proprietary advantages gained thereby, and the concern has extolled, through advertisements and the radio, the virtues of acetylsalicylic acid for the self treatment of many disorders. Other firms have done the same. Probably no other drug, as widely used, has had fewer deaths reported following its use. Fortunately, most persons who take acetylsalicylic acid, in common with other salicyl compounds, experience a warning sign (tinnitus) if overdosage is imminent, so that the drug may be discontinued before these persons become seriously poisoned. In spite of the tremendous amount of self medication with aspirin in this country, comparatively little poisoning has been reported. No doubt, much harm indirectly has probably followed its indiscriminate use, in that conditions for which it was used were not remedied.

Since introduction of aspirin forty-one years ago by Dreser, many reports have appeared on the adverse effects which may follow its unwise use. These have included depression of the heart, habit formation, miscarriage in pregnancy, and idiosyncrasy causing such alarming symptoms as urticaria, pruritus, erythema and generalized angioneurotic edema. Cutaneous eruptions of various forms are not unknown, and even ulceration and gangrene have been attributed to its use. Because of the irritant action of the products containing the salicyl group on renal epithelium, acetylsalicylic acid is contraindicated in nephritis. Other persons especially susceptible to undesirable effects of the drug are drunkards and persons with diabetes. In the latter groups, adverse effects show a special relation to the nervous system.

Now comes a report [1] from the London *Lancet* indicating that a surprising number of deaths reported in England are due to this product, much out of proportion to the experience in the United States. According to this source, in England and Wales in 1938 the number of deaths due to poison was reported to be 735, of which 591 were suicides, ninety-two accidental and the remaining doubtful. The agent responsible for forty-three of the suicides, for eight of the accidental and for fourteen of the doubtful group of deaths was said to be aspirin; thus aspirin was reported as the cause of death in sixty-five of 735 fatal poisonings. In 1937 about the same number of deaths from poison occurred in this area, with aspirin listed as the responsible agent in sixty-one cases. In 1936 the number recorded was about half of the number in 1938, which would indicate that aspirin caused about 150 deaths in three years in England and Wales alone. The *Lancet* considers it "curious" that a drug which caused sixty-five reported deaths in one year is not classified as a poison. An antidote is not known for the treatment of cases of acute poisoning. Therapeutic agents which may be harmful in excess dosage have recently been subjected in Great Britain and in some areas in this country to certain restrictions to prevent excess sale to the public. Perhaps further attention should be given to acetylsalicylic acid (aspirin) if it is capable of causing as many deaths as have been reported in Great Britain.

Another member of the salicylic acid family which does not have altogether the same side reactions is methyl salicylate, well known commercially as oil of wintergreen. Approximately two years ago THE JOURNAL published an article on methyl salicylate poisoning in which Baxter, Hartwell and Reck [2] reported two deaths in children following the accidental swallowing of oil of wintergreen. The authors also referred to an article in the *Archives of Pediatrics* wherein twenty-eight cases of methyl salicylate poisoning were reviewed by Lawson and Kaiser,[3] who added another case of death following the use of methyl salicylate as a counter-irritant. In the twenty-eight cases reported by Lawson and Kaiser there were ten recoveries and eighteen deaths. It is also interesting to note that, in the report of the Registrar General in Great Britain on Poisoning, methyl salicylate was shown to be responsible for three deaths in 1938, four in 1937 and four in 1936. Because of two recent deaths of children in Canada the Canadian Council of Health [4] is considering classifying methyl salicylate as a poison. The mortality among the children has been as high as 60 per cent, even though only a small quantity has been taken. Evidently much more attention should be given to the toxicity of these rather common products which are used both in the home and in the practice of medicine.

1. Aspirin as a Poison, Lancet **1**: 1091 (June 15) 1940.
2. Baxter, E. H.; Hartwell, R. M., and Reck, L. E.: Methyl Salicylate Poisoning, J. A. M. A. **111**: 2476 (Dec. 31) 1938.
3. Lawson, R. B., and Kaiser, A. D.: Arch. Pediat. **54**: 509 (Sept.) 1937.
4. Pharm. J. **145**: 5 (July 6) 1940.

Current Comment

MILITARY PREPAREDNESS

Elsewhere in this issue under the heading of Military Preparedness appear the minutes of the special session of the Committee on Medical Preparedness of the American Medical Association which called in Chicago a conference of all the chairmen representing the different state organizations for military preparedness. There appear also the minutes of the meeting of the committee itself, held the same day. In attendance also were representatives of the United States Army and Navy Medical Corps, the United States Public Health Service and the Selective Service organization. The information supplied was of the utmost importance in developing plans for the organization of the medical profession in relationship to mobilization of men for military service. Every physician should read carefully these minutes in order that he may be aware of the answers to many of the questions which are now pouring into the headquarters office. Every physician is anxious to do his part. Every physician is likely to be asked also as to exemption of various groups of the population, physical examinations and similar subjects. Most of the answers will be found in the material published in this issue. If not, at least there will be an indication as to the proper agency to be consulted for a proper answer.

THE EFFECT OF INDUSTRIALIZATION ON MORTALITY FROM TUBERCULOSIS

In a series of studies of mortality from tuberculosis and industrialization with special reference to the United States, Wolff [1] has presented statistical data obtained from many sources. The disease continues to retain its important place as a cause of death in spite of a remarkable decline. This is due, Wolff believes, to two causes: first, the prevalence of tuberculosis in persons in the prime of life; second, the fact that, as a chronic infectious disease, tuberculosis becomes active at any time when environmental conditions become unfavorable for large groups of people. Such was the experience of the World War in all those countries directly or indirectly implicated in war distress. Surprisingly, however, increasing industrialization has been accompanied by a decline in mortality from tuberculosis, probably because of the general improvement in standards of living for the bulk of the people brought about by industrialization. Density of population itself furthermore does not determine the mortality from tuberculosis but there is some other causal factor probably connected with crowding and social environment. It is therefore rational, Wolff believes, to aim preventive measures largely at improving social environment. For the time being at least the level of mortality from tuberculosis may be considered an index of hygienic and social culture. By this standard the United States ranks first among the world states even when the high mortality of the Negroes is included.

1. Wolff, Georg: Tuberculosis Mortality and Industrialization, Am. Rev. Tuberc. **42**: 1 (July, Aug.) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

CONFERENCE ON MEDICAL PREPAREDNESS

Held at American Medical Association Headquarters, Sept. 20, 1940

Because of the illness of Dr. Irvin Abell, chairman of the Committee on Medical Preparedness, Dr. James E. Paullin was elected to preside. A telegram from Dr. Abell said: "Am distressed in not being able to be present today at what I regard as an extremely important meeting. Since the A. M. A. has voluntarily assumed the responsibility for surveying the qualifications and availability of the medical personnel of the country, nothing should be allowed to interfere with the successful and prompt fulfilment of this self-imposed obligation. In the degree in which we succeed we shall be judged, and our responsibility to the American Medical Association demands 100 per cent fulfilment. Such states as are in arrears should be made to realize their duty and, if necessary, change in committee personnel made to give some assurance of discharge and fulfilment of duties assigned. With assurance of my hearty cooperation in all that you do, Sincerely, Irvin Abell."

The Coordinating Committee

Dr. Olin West, Secretary of the American Medical Association, reported the text of the executive order by the President creating the Coordinating Committee as described in THE JOURNAL last week.

The Medical Examining Function under Selective Service

Col. Charles B. Spruit gave the available information describing the work of the physicians under the Selective Service Act. This paper was published in full in THE JOURNAL last week.

Dr. Samuel J. Kopetzky, New York, stated that the medical profession had been completely organized for service in the selection of young men for training under the Selective Service Act. The governor of the state had conferred with him as chairman of the Preparedness Committee of the American Medical Association in New York. The state had been divided into eight police districts with main headquarters in Albany and separate headquarters in New York City, the mayor of New York City being in charge of these activities and the rest of the activities of the state under the direction of the Adjutant General in Albany. Two nominees were selected for each draft board of the state, and the governor selected a physician for each 30,000 of the population in the state to serve on the local draft board. Similar arrangements were made for the city after conference with the five county medical societies in Greater New York. Arrangements were also made to set up medical advisory boards to pass on appeals from decisions of the physicians of the local draft boards. Each medical advisory board contains a surgeon, an internist, an ophthalmologist, an otolaryngologist, a psychiatrist, an orthopedist, a roentgenologist and a dentist. The mayor and the governor of New York also requested lists of physicians with a broad, communal point of view to serve with draft boards as members of the board rather than as physicians. Contact was made with the state dental association and with the state pharmaceutic association, so as to provide the necessary members of the boards from these professions.

Function of Induction Boards

Col. Albert G. Love, United States Army Medical Corps, said that registrants under the Selective Service would first be passed on by the members of the board before they were referred to the physician. In 1917 one man out of every five or six examined was unable to go because of some economic or matrimonial reason. Thus a tremendous amount of unnecessary work was placed on the shoulders of the doctors. It is proposed on this occasion to have the man passed for all other reasons before submitting to the medical examination. A different plan would involve the examination of 16,500,000 men instead of the examination of 4,000,000. Every effort is being made to examine the man as closely as possible to his home so that he will be away from his home and job or position as short a time as possible. There will be 100 induction boards to make final examinations of registrants before they are sent to cantonments and camps. Selection and organization of these boards will be determined by the corps area commander. There will be one or more of these boards for every state, depending on the population. On each of these boards there will be one orthopedist, one general surgeon, three internists, two ophthalmologists, one otolaryngologist, one neuropsychiatrist, one clinical pathologist and one dentist.

The United States Public Health Service has taken over the work of collecting and making serologic examinations. X-ray examinations of the chest will not be made at these examining points for all men but will be made only as required in order to determine definitely whether a man is physically fit. Only such laboratory work will be done as the examination of sputum and urine. If more technical laboratory work is required, it will be delegated to local medical facilities. After the man is inducted and brought into camp a general x-ray examination of the chest of each man will be made, with the preparation of two permanent films. A hundred x-ray machines for the taking of such films have been ordered and will be delivered within the next six months.

Colonel Love stated that there are approximately 15,000 reserve officers now in the Medical Reserve Corps. The Army will require 8,000 physicians in addition to those now in the Army Medical Corps and those in the National Guard. If the 8,000 are taken from the Reserve Corps, it will be necessary to rebuild the Reserve Corps. In the setting up of the induction boards it is proposed to use civilian specialists as well as reserve officers. The Committee on Medical Preparedness will be associated with the development of the necessary personnel.

Medical Officers for the Navy

Capt. D. G. Sutton, United States Navy Medical Corps, pointed out that the Navy was not involved in any way with the problem of Selective Service at this time. Should the Navy become involved, the physical standards will be about the same as those set forth by the Army. All naval recruits are centralized in areas known as Naval Training Stations, of which there are eight or ten throughout the United States. The maximum number of men required by the Navy is about 500,000. He asked particularly that interest be stimulated in the Naval Reserve Corps as far as physicians are concerned. There are now approximately 1,100 vacancies in the various categories in the Naval Reserve Corps, that is of commissioned medical officers, and about 208 vacancies in the regular service. The Navy prefers the younger men who are recent graduates from class A medical schools.

Instead of planning for the large x-ray film of the chest, the Navy is using the small 25 mm. film.

DISCUSSION

The subject of the selection of physicians for the induction boards was discussed by Drs. Holman Taylor, Texas; W. C. Dixon, Tennessee; Stanley H. Osborn, Connecticut; F. X. McGovern, District of Columbia; John F. Sharp, Utah, and W. R. Brooksher, Arkansas.

Status of Physicians on Draft Boards

In reply to questions raised in this discussion, Colonel Spruit said that a member of the Selective Service Board will be a government official of the Selective Service. Physicians on the boards will not be paid. Colonel Spruit quoted the policy of Selective Service:

"There is a strong feeling in Congress and throughout the nation that, inasmuch as men are being called to military service at great personal sacrifice, Selective Service officials should be men willing to make an important sacrifice by contributing voluntary service, and that a process based on the devotion to the national interest should not deteriorate into a job-holding organization.

"It appears very probable, therefore, that no compensation will be provided for members of local boards, boards of appeal, medical advisory boards, examining physicians, additional examining physicians or other similar officials. Clerical employees will unquestionably be paid and will be thoroughly competent in order to free officials from petty clerical routine and leave them free to devote their time to their important responsibilities."

Provisions have been made to furnish supplies utilized and required in physicians' examinations in the Selective Service process and to pay for those procedures necessary for the determination of physical fitness, such as laboratory or x-ray examinations. Colonel Spruit requested the Committee on Medical Preparedness to establish a fair list of prices for technical examinations, which will be paid for from government funds after the due amount of paper work has been accomplished.

Colonel Spruit indicated that the fall quota for the Selective Service would be about 400,000 men, divided equally between 6,500 local examining boards, which would require about sixty men to be selected by each board. Applying the percentage of rejections, about ninety men would come before the physicians of the local board for physical examination. Since, however, the examinations are to be spread over a period of from three to four months, the total requirement of examination for each local board would be between twenty and thirty men a month.

The policy has been adopted that only doctors of medicine will be utilized in carrying out the medical functions of the Selective Service.

No plans have been made for taking men with correctable defects into the Army. Colonel Spruit said it would be a broad and desirable humanitarian procedure if the Army were able to take in the defectives of the nation secured by the draft and fix them up so that they could go back into civil life as good sound men. However, the purpose of the act is to get men to do twelve months of training and service, after which time these men go into the reserve for a period of years. The Army wants men who are immediately capable of undertaking full military service and not those who are inducted and then sent to hospitals for treatment before they can begin training. Men with correctable defects may be deferred by the local board, subject to a voluntary correction of the defects if the young man cares to have such correction made.

It is contemplated that the physicians who are members of induction boards may be compelled to travel in carrying out their services.

The Reserve Corps

Colonel Love, United States Army Medical Corps, pointed out that the Adjutant General, at the request of the Surgeon General, has sent out to every corps area commander who works through the corps area surgeon a request to send to every reserve officer a questionnaire in which he is asked whether he desires to accept military service at this time. If he cannot accept military service at this time, he is asked to put down the reason for his refusal. The army requires definite information as to the men who may be available for military service with the least possible disruption of the civilian medical services as far as teaching and hospitals are concerned. Doctors are required for 1,400,000 men who will be in training. When physicians are called under the Selective Service Act, they will have special status. Any man who is eligible for Selective Service may apply now for a commission in the Medical Officers' Reserve Corps. If he does not apply for a commission and later is selected for service and taken into the Army, he will then be given an opportunity to qualify for a commission. He will, however, avoid registration under the Selective Service Act if he applies at once for a commission in the reserve corps.

The subject of examinations of interns, residents and medical students was further discussed by Dr. F. L. Smith, Minnesota; Dr. James E. Paullin, Georgia, and Dr. Harvey B. Stone, Maryland. Instructions have been sent, said Colonel Love, to the effect that an intern who has not completed one year of service is not to be considered eligible for active duty. Moreover, second year interns have been placed on a low priority list and are not to be disturbed if this can possibly be avoided.

Physicians on Induction Boards

In reply to a question, Colonel Love stated that physicians who are serving on induction boards, with the exception of the officer in charge of the board, will be on temporary duty. Reserve officers who are available will be called under a temporary duty status. Civilian physicians will be on a per diem basis and will be used as long as their services are required. Civilian physicians will be without military status. It is planned to utilize the services of those who, on account either of age or of physical deformities or because of reasons affecting their civil life, cannot go to military camp but are willing to engage in this type of service and thus do their part in the field of national defense.

The work of the physicians on the Selective Service Board, as developed in Indiana, was described by Dr. Charles R. Bird.

Arrangements were made to send to the headquarters of the American Medical Association complete lists of the names of all physicians serving on Selective Service local boards and advisory boards. Dr. Olin West pointed out also the need for supplying the headquarters office a complete list of all medical reserve officers in each state. Further discussion was supplied by Dr. Hugh H. Trout, Virginia, who requested information as to the manner in which the list of questionnaires was to be made complete. Dr. Arthur T. McCormack, Kentucky, described the activities carried on in that state, which now has the record of having secured the greatest number of returns. Dr. Holman Taylor, Texas, discussed the recording and status of physicians associated with the National Guard.

Exemptions of Medical Students, Interns and Residents

Dr. Olin West pointed out that many letters had been received in the headquarters office from interns, residents and medical students, as well as from faculties of medical schools, inquiring as to the status of these groups under the Selective Service law. Dr. Morris Fishbein asked as to the status of interns under the Selective Service and as to whether or not they would be given an opportunity to qualify for a commission in the Medical Reserve Corps. It was pointed out that the Selective Service Act exempts young men in universities in training for degrees in science and that many medical schools do not award a diploma until after the internship is completed. It was pointed out also that the certifying boards for the various specialties would have to arrange in some manner to provide for the resident who had completed one or two years of his residency or fellowship and who was called to military service. In response Colonel Spruit said:

"I shall have to descend to the status of a guardhouse lawyer, since this is now a matter of the interpretation of the law. Let me read you a brief description of what the law says. Now the law uses two terms: one of them is the word 'exemption,' which means to clear out; the other is the word 'deferment,' which means to put off. And so with those two barnyard definitions we will proceed.

"The first exemption that is open or that will be conferred upon members of the medical profession is an exemption from registration. Obviously, if you don't get your name on the book, they can't find you. So if you are not registered, if you are exempt from registration, you will not be called. And the exemptions from registration comprise the warrant officers and enlisted men of the Regular Army, Navy, Marine Corps, Coast Guard, Public Health Service, the federally recognized active National Guard, the organized reserve of the Regular Army,

the enlisted men in the Naval Reserve, the Marine Corps reserves, cadets of the U. S. Military and Naval academies, cadets in the Coast Guard academies or men who are accepted for admission thereto, and cadets of the advanced corps of the R. O. T. C. in the Army or in the Navy.

"Now, we have twenty-three medical R. O. T. C. units in the country, which means that those men in there who are in their junior and senior years will be exempt from registration. All students presently entered on college courses leading to a degree in the arts or sciences will be deferred until July 1, 1941, which means that all students who are entering courses leading to a degree are deferred for this year. However, they must register. If I understand the law correctly, then the R. O. T. C. medical students don't have to register, the assumption being that we are going to get them in the reserve corps at graduation.

"When we come over to this question of deferments, we come from a definite classification to a lot of general terms. Let me read you the statement in regard to no deferments. The law says: 'There will be no deferments made in the case of any individual except on the basis of the status of that individual, and further that no deferment shall be made of individuals by occupational groups or of groups of individuals in any plant or institution.' In other words, there will be no blanket deferments except those authorized by the law.

"'It will thus be seen that the deferment of any individual whose exemption or deferment is not specifically provided by law will be decided by local boards on the merits of the case and the demonstration of the necessity for deferment. It is believed that such necessity can be demonstrated for residents and interns in hospitals, for key technical personnel in hospitals and laboratories and for officials in state, county and local health departments, and similar participants in matters of the public health.' That is a very broad provision upon which I shall not attempt to elucidate at this time.

"'Furthermore, men may be granted exemption under the judgment of the local boards who are found, as individuals, to be necessary in industry, agriculture or some other occupation in order to maintain national health, safety or interest.'

"I feel, as every one in the room must feel, the dire necessity of providing for the continued training of medical education in the country. Those students will be deferred for another year, but each case is going to have to be settled, under the present law, on its own present merits. As far as the men in hospitals are concerned, I would like to hark back to what I said before; namely, that there are three ways in which an appeal can be made to the classification of any man: the individual himself, his employer or the government agent who is appointed to look after the interests of the government and of the community at large. So that if the man himself doesn't appeal but if the hospital in which he is an intern or a resident thinks that he is vital and can support their case, they can request an appeal."

Dr. Edgar H. Greene, Georgia, inquired as to the status of public health officials who are also members of the reserve corps. He inquired also as to the possibilities of additional R. O. T. C. units in medical schools. Colonel Spruit pointed out that authority must be gotten from the War Department for the establishment of additional R. O. T. C. units, particularly since an appropriation would be required from Congress. He felt that this was a feeble reed on which to lean for the deferment of medical students. All men who are on the active list of the organized reserves are exempt from registration; that is, any one who is in good standing and an officer in the reserve corps will not be registered. The question was further discussed by Drs. Holman Taylor, Stanley H. Osborn and Charles H. Henninger, Pennsylvania, with respect to exemptions of public health officials.

Dr. W. D. Cutter reported on the results of the questionnaires sent to medical schools asking them to furnish the classifications of the faculty with regard to those essential to the continued conduct of the school, a second group whose presence was desired but who were less necessary, and a third group of those who could readily be spared for military duty. Fifty-seven schools have already sent lists of the faculty thus classified. Others are completing the lists just as soon as members of the faculties return from their vacations.

Dr. Alexander S. Begg, Massachusetts, reported on the work of the Committee on Mobilization of the Association of American Medical Colleges. Dr. Begg analyzed the Selective Service Act as it relates to the students. He felt that under the law deferment is made possible on presentation of information to the Selective Service boards. He also discussed the question of hospitals which are not teaching hospitals but which are necessary for community health.

Serologic Tests of Selective Service Registrants

Dr. Thomas Parran said that he thought it desirable to provide opportunity for a Wassermann test to the 16,000,000 registrants, who would report at 143,000 registration booths. Men of the ages of 21 to 35 would represent 70 per cent of the active syphilis of the nation. Some 900,000 cases might be expected to be found if it was possible to make routine tests of the entire 16,000,000 men. Of the 900,000 cases with positive reactions, about 300,000 would be infectious, he said. Difficulties represented were the lack of physicians capable of supplying 143,000 registration offices with men capable of taking blood and the volume of serologic tests which would be necessary. The American Legion had offered to give help in the clerical and other necessary work and to encourage the registrants to take the tests. Dr. Parran discussed the incidence of syphilis in this age group and proposed the following plan:

"Specifically it is proposed that the collection and examination of specimens be accomplished as follows:

"1. A team of one or more doctors and nurses to be provided at each registration point and to be responsible for the collection of the specimens. Local and state health departments should be able to obtain the services of the physician and provide the nurse in cooperation with the local and state medical societies without cost to the selective draft board.

"2. The blood specimens with the identification blank properly filled out to be sent to the nearest public health laboratory where serologic tests for syphilis are performed. Such laboratories should be notified, if possible, ten days to two weeks in advance of the approximate dates of registration in order that routine serologic work may be set at a minimum during the registration.

"3. The men whose blood specimens proved to be negative by serologic test should be notified directly regarding the laboratory findings. The men who have positive or doubtful serologic tests should be directed by mail to report to the physician or clinic named on the original identification slip which was forwarded from the collection point to the state laboratory. The positive or doubtful report should be sent to the man's physician or clinic in order that the proper physical examination may be performed to supplement evidence obtained through serologic examination of the blood and necessary to confirm the diagnosis of syphilis.

"4. Individuals found to be infected with syphilis may according to circumstances arrange for treatment either from their own physician or from public clinics, of which there are approximately 2,500 at various places throughout the United States."

He stated that the plan has the approval of the Subcommittee on Venereal Diseases of the National Research Council, and it was hoped that the American Medical Association would encourage the plan through its affiliated state and county medical societies, thus securing the cooperation of the physicians.

In the discussion Dr. Samuel J. Kopetzky stated that the matter had been brought before the Medical Society of the State of New York and that it was the feeling of the council that the Selective Service Act, with its registration and its examination, is a new procedure and it would be unwise to complicate it with public health activities. Such complication would confuse the public and give newspapers and other agencies not favorable to Selective Service an opportunity to condemn the entire procedure. It was felt, however, that a serologic program could be conducted for the 400,000 men who would be accepted and inducted into service. Dr. George M. Smith, Connecticut, and Dr. Arthur T. McCormack, Kentucky, commented on the plan, the statement by Dr. McCormack ending with a recommendation for its adoption.

AFTERNOON SESSION

Resolution on the Rehabilitation of Men Disqualified for Service

Dr. Parran of the U. S. Public Health Service presented a statement prepared by a committee of the Conference of State and Territorial Health Officers concerning the rehabilitation of men found disqualified for service by reason of physical defects. The following resolution, offered by the committee of the Conference of State and Territorial Health Officers, was read. Dr. Parran suggested that the resolution be a possible subject for future consideration by the Committee on Medical Preparedness:

Resolved, That persons who are otherwise found to be satisfactory and available for induction into the land or naval forces of the United States for training and service as provided by the Selective Service Act but who are deferred because of physical defects or ailments which are readily amenable to treatment and cure as stipulated by regulations which may be prescribed by the President may, on application to the Public Health Service, be considered and accepted for such treatment as beneficiaries of that service for the correction of such physical defects or ailments.

Relations of Committee on Medical Preparedness to Governmental Agencies

Dr. Morris Fishbein stated that a chart is being prepared which will clearly show the relation of the various bodies and committees which have been formed, indicating also just where official power lies, where advisory power lies and which bodies are without authority. He said that, while various governmental agencies had requested the American Medical Association to aid them in mobilizing medical personnel, the Committee on Medical Preparedness appointed by the Association for that purpose has no authority to order anybody into service but can only find out if an individual wants to go into the service and furnish such names to the government. The punch card system on which the Committee on Medical Preparedness is working is of real value only if it is complete. Obviously a good job cannot be done if there is on the punch cards only 75 per cent of the doctors who are available. The very first job, therefore, Dr. Fishbein said, that lies before the state chairmen when they return home is to obtain the return of all the questionnaires of the medical preparedness committee which have been sent out to individual physicians, in order that the punch card system may be complete. This work of mobilizing medical personnel is greatly complicated by the fact that there are innumerable medical organizations in the field; for example, some of the boards in the specialties have urged that physicians be not recommended for service on any board as specialists unless they hold a certificate from the examining board. This would be most difficult to follow in some states. Other complications that were mentioned were the needs of industrial medicine, the promotion of public health activities in relation to the military emergency, and the question of medical students. The needs of the military service obviously come before every other demand.

Intensification of Medical Education

Dr. William D. Cutter said that the Council on Medical Education and Hospitals as yet has no specific plans for the intensification of medical education in relation to the Conscription Act. The Council has not met since this bill was enacted. Certain medical schools, however, have been considering the lengthening of their school year so that the course can be completed in three calendar years rather than in four. Some schools are already operating on that plan and it would be very difficult for others to adopt that plan.

Dr. Alexander S. Begg pointed out that a group interested in the venereal disease problem had sent a memorandum to all medical schools suggesting an intensive two weeks course be offered to physicians who are able to go into the service. He suggested that probably the orthopedists and various other groups might want short intensive courses given also.

Dr. Olin West brought out that various groups are attempting to exert influence in Washington in behalf of plans for the extension of what they call medical education. Indeed, a bill has been introduced in Congress designed to care for the interests of one unrecognized medical school. Certain commercial groups are trying to exert pressure in the same direction in Washington. Great pressure is being brought in behalf of certain cult practitioners in an endeaver to have them recognized in the same way as doctors of medicine are to be recognized.

Physicians to Serve the Civilian Population

Dr. West stated that under the plan adopted by the Committee on Medical Preparedness it is provided that county medical societies shall be active in the selection of physicians whose services would be more valuable among the civilian population at home than they would be if these men were called into active military service. In some states it appears that no county committees have been appointed. Dr. West said that this matter of appointing county committees should receive prompt consideration at the hands of the state committees.

DISCUSSION

In the discussion Dr. Samuel Kopetzky said that in each county of the state of New York there is already a medical preparedness committee which places a confidential notation on every questionnaire as to the value of a physician, as to his need in the community or whether he is better suited to serve in the federal service, as a reserve officer, as a public health officer, in industrial medicine in plants, in the Home Guard or in some other category.

Dr. Roy W. Fouts of Nebraska said that the plan of appointing county committees would not work in Nebraska, as there are some counties in that state which do not have even one physician, much less a county medical society, and that the same holds true for a number of the Western states. Dr. Fouts suggested that this matter be handled in Nebraska through the councilor districts rather than on an individual county society basis.

Dr. Holman Taylor of Texas said that he was one of a committee of this kind during the last war and that they went into communities where there were doctors to spare and induced those doctors to go to other sections of the state of Texas where doctors had been sent into active military service. He raised the question whether these county society committees would actually have the authority for making such decisions as this; that is, would the higher authorities endorse the county society method of selecting those that are best qualified to serve among the civilian population.

Dr. Charles W. Maxson of Maryland read a questionnaire which one of the county chairman in Maryland had sent out to every doctor in that county.

Capt. D. G. Sutton, U. S. Navy Medical Corps, suggested that this is a national question and comes within the purview of the new coordinating committee established by executive order. This committee, he said, could outline a definite policy that could be applied to all the states after having received from the states information that would serve as a background for determining the final action.

Colonel Love said that a careful reading of the orginal proposal submitted by Colonel Dunham before the House of Delegates of the American Medical Association in New York last June would clear up many of the points being raised at this time. The Surgeon General's Office has proposed to the War Department that all calls for physicians beyond those who are available in the National Guard and in the reserve corps would be supplied through the Committee on Medical Preparedness of the American Medical Association; for example, a corps area commander who requires a surgeon or internist or some other kind of doctor would transmit his call to the Committee on Medical Preparedness of the American Medical Association in Chicago. The reason for that plan is that there may be many more troops in a certain corps area than can be supplied with the number of doctors from that corps area, but when a call comes into the central committee for doctors they can say to some state that it is their turn to furnish the type or types of doctors required. The Surgeon General's Office has suggested to the Secretary of War, as well as to the Committee on Medical Preparedness, that the Surgeon General have representatives on duty with this committee in Chicago so that he may give official sanction to recommendations made by this committee, which in turn will be transmitted to the state and county medical societies.

Dr. James R. Bloss of Huntington, W. Va., said it could be made a simple matter for the doctors of the country to take

care of the civilian population. In the World War he and his associate asked each new patient that came to their office "Is your doctor in the service? and if the patient said yes, his name was written in red ink in their books and any amount collected from the patient was sent to that doctor's family. When physicians who were called into service returned to the community, he said to their patients "Your own doctor is back now, go over and see him." Dr. Bloss and his associates feel that this question is a personal matter to a large extent.

Dr. Olin West again emphasized the importance of completing the organization of medical preparedness committees in the county societies, which he hopes will be perfected soon in every state. There will be some things in each local situation that will have to be carefully supervised by the state committees on medical preparedness.

Dr. F. Webb Griffith of North Carolina inquired if the states are going to get duplicates of the punch cards of the central Committee on Medical Preparedness. Dr. West replied that, in view of the great pressure of trying to get this information transferred to these cards, it was doubtful whether the committee could undertake to provide the states with duplicates at any time very soon. He pointed out that the county committee should know better than anybody else which physicians can best stay at home and who might be essential for civilian service.

Dr. F. L. Smith of Minnesota said that to date they had received back 83.5 per cent of 2,600 cards sent out to physicians in the state. It is necessary, he said, to make a personal canvas, and this was being done in Minnesota through the county societies, which with the councilors have a list of all physicians in their district. In Minnesota they have a committee comprising one member for every district so that between the representative of the military committee, the county chairman and the councilor they expect to get the information desired from every physician in the state, even if necessary to make a house to house call. Minneapolis and St. Paul are already sending their representatives to interview personally men who have not returned their cards.

Dr. J. N. Davis of Idaho asked What is an acceptable per capita need of the civilian population for physicians? Dr. Olin West said that the question is difficult to answer. Should an epidemic develop as it did in 1918, there is no way of figuring out the per capita need for physicians. In a situation of that kind and in less serious situations among the civilian population we have to meet the situation that exists, and all that one can do is to do the best without reference to per capita needs.

Dr. George H. Phelps of Wyoming said that a plan which would work in one state might not work in another state. It may be well, he said, to leave this to the discretion of the Coordinating Committee in conjunction with the Committee on Medical Preparedness to work out definite ideas which can be submitted to the various states.

Dr. Fishbein referred to Colonel Love's statement at the morning session that the immediate needs probably can be taken care of out of the reserves as long as we are not actually engaged in war. Should the government declare war, this problem could not be handled without some sort of conscription that would reach physicians and provide authority to reach those physicians who are actually needed in the service, as well as to give authority to somebody to declare just who ought to stay at home and who ought to go into active service. The time is not ripe, Dr. Fishbein said, to confer that authority on any one. Dr. Olin West emphasized that while we may not be going to decide at present just who is going to stay at home and who isn't, we ought right now to be working out a plan to provide for the civilian and the industrial needs, and to this suggestion Dr. Arthur McCormack of Kentucky agreed.

Plans to Secure Return of Physicians' Schedules

Dr. R. G. Leland, whose department in the headquarters of the American Medical Association is conducting the survey of physicians for the Committee on Medical Preparedness, pointed out again the necessity for a 100 per cent return of schedules that have been sent to physicians. No state as yet had reached that point. Various means have been used by different states to secure a complete return of schedules, but it will be necessary to exert still more ingenuity and pressure on those who are tardy in returning their schedules. These schedules are needed even though the physician has supplied the information to the Army or Navy as members of the Officers Reserve Corps. Only by having a complete list will the Committee on Medical Preparedness be able to serve the armed forces in the best manner. Dr. Leland believes that ultimately personal visitation committees will be required in most communities to follow up those men who do not respond with their questionnaires. In their effort to complete the survey of physicians, many states have asked the committee for lists of physicians who have already returned their schedules in order that they might learn the names of those who have not returned them. The preparation of such lists entails much work, for it is necessary to check all of more than 100,000 schedules that have been returned. It is especially requested that state and county committees do not ask for such lists, as that would be especially time consuming. If there are other methods which are better than preparing a list of those who have not responded, anything that can be done to assist the states in getting a full return to their questionnaires will be gladly done.

In reply to a question from Dr. Charles R. Bird as to how soon the checking of the state lists could be had by individual states, Dr. Leland replied that it probably would take from ten days to two weeks at least to make this check. In response to the question whether they have a list made up of those who have filled out the questionnaires, the answer was yes, except in a few states in which the number of returns is less than 50 per cent.

Dr. Hugh H. Trout of Virginia said that a great deal of this work in his state had been completed with the aid of the woman's auxiliaries. The women have gone out to their doctor husbands and friends and had them turn in the necessary information.

Another plan has been adopted for states in which there are comparatively few physicians, namely the sending out directly from Association headquarters of a second request for the information desired. That has been done in seven or eight states and the response to the second request has been very satisfactory.

Colonel Spruit pointed out that the regulations on physical examinations have recently been printed by the army and that he hoped that the examining boards would read and apply them.

Dr. Stanley H. Osborn asked whether the different state chairmen can get from the Committee on Medical Preparedness a list of the physicians who would volunteer for active service. Dr. Leland replied that on request a list could be prepared of those who are willing to volunteer for service.

Relation of Committee on Medical Preparedness to Other Agencies

Colonel Love stated that the Surgeon General's Office feels that the American Medical Association should be able to speak for the medical profession and that it is the wish of that office at present to coordinate, as far as possible, the work of medical preparedness through the central Committee on Medical Preparedness appointed by the American Medical Association.

The Neuropsychiatric Problem

Dr. Parran stated that, if the methods of physical examination to be followed in the current emergency are the same as those followed in the World War, and if no more of the potential psychiatric cases are excluded than in the last war, then we can expect 2.2 per cent of all men inducted into the service to become wards of the government and to receive treatment and compensation at its hands for the next twenty years following their induction. An estimate of the cost to the government of every case of this kind, including the cost of buildings, compensation and other expenses involved to take care of them, amounts to $30,000 per case. If the same figures apply to the men to be inducted for training in the next few months, the total cost over the next twenty-two years to the government for the probably 22,000 neuropsychiatric patients would be 660 million dollars. Dr. Parran pointed out that in the last draft, in many places, the draft boards were too willing to send to the army the problem boy, the shiftless fellow, the ne'er-do-well, and that it should be possible for the local draft boards, the medical advisory boards and finally the induction boards to give more attention to this particular problem, to which he hopes the Committee on Medical Preparedness will give further consideration.

New York's Plan to Protect the Doctor in Active Service

To protect the doctor who goes into active military service, and to make it easier for him to fulfil that obligation, New York has adopted, Dr. Kopetzky said, the "Bower plan," whereby the physician going into the service notifies his county society officers, who set up a fund in which the money collected by the substitute doctor is deposited minus a certain percentage for overhead, and that fund is administered by the county medical society. Certain hospitals also have established funds within the hospital in the same way. Thus the patients of the physician who goes in the service will be taken care of by those who remain at home and the physician or his family will get the money collected by the substitute physician, less a certain per cent for overhead. Under a tax ruling in the third tax district in New York, these funds are taxable as income and when the funds are distributed to the doctors who go into the service they must register it in their income tax returns and it is again taxed. Now what is needed is an executive ruling from the Secretary of the Treasury that such funds shall either be taxed at the source or at the time the recipient gets the money. Dr. Kopetzky requested that the Committee on Medical Preparedness take this matter up with the proper treasury official, so that it may be straightened out. In reply to a question from Dr. Charles E. Hunt of Oregon, it was said that the amount deducted for overhead in some instances is 5 per cent but that it depends entirely on the local conditions, and in the case of some of the sponsored hospitals there will be no overhead charge.

Short Intensive Training Courses

The subject of short intensive training courses for doctors who are going into active service brought forth an extensive discussion. Colonel Love said that there ought to be several short intensive courses of training and that the Committee on Medical Preparedness might coordinate them and carry those courses of training through the medical schools and hospitals. Dr. Fouts suggested that all doctors up to 50 or 55 years of age who are physically fit be given a short intensive military training course. Dr. Taylor of Texas approved the suggestion. Dr. Robert Mueller of Missouri said that in the last war the percentage of decorations which doctors received in the army was greater than that of any other similar group of officers throughout the United States forces.

Dr. Edgar H. Greene of Georgia believed that the older physicians should not be subjected to intensive physical hardships but that the young physician should. The older physician who had no military training, however, should be given a course in military affairs pertaining to the manual of the medical department and the army regulations, in order to become acquainted with the paper work; he recommended in seven districts of the state of Georgia that they set up courses to instruct interested physicians along this line.

Interns and the Reserve Corps

After conferring with Colonel Love, Dr. Cutter suggested that, as soon as orders have been issued permitting the increase in the Medical Reserve Corps, it might be advisable to notify all hospitals approved for the training of interns to inform the interns that an opportunity is given them to request commissions in the Reserve Corps with the understanding that they will be expected to complete their intern service before being called into active duty. If that plan meets the approval of the Surgeon General's Office, Dr. Cutter, in behalf of the Council on Medical Education and Hospitals, said he would gladly bring it to the attention of each one of the nearly 1,000 hospitals in the country approved for intern training.

Colonel Love, in reply to a question, stated that commissions will not be granted to applicants unless they are graduates of class A medical schools.

Certificates for Physicians Compelled to Stay at Home

Dr. Harrison Shoulders of Tennessee suggested that some sort of token or certificate be issued to physicians of military age and physically fit who had volunteered for service but were compelled by the proper authority to remain at home where their services were needed. A motion was adopted to the effect that the Committee on Medical Preparedness design and award a badge for those physicians referred to who cannot enter the active military service.

Lists of Local Examining Boards

In reply to a previous question concerning tentative lists of men assigned to local examining boards, Dr. Greene said that all one has to do to get these lists is to go to the adjutant general's office in his state and find out there what doctors have been selected for these local boards, as a mobilization plan has already been set up for several months in the states. These lists, therefore, can easily be prepared and sent in to the Committee on Medical Preparedness in Chicago.

Brief Conferences of State Chairmen

After announcements from various state chairman of requests for brief conferences with the other state chairmen in their corps areas immediately following this meeting, and that the Committee on Medical Preparedness would hold an official meeting at 6:30 p. m., the conference meeting was adjourned.

COMMITTEE ON MEDICAL PREPAREDNESS

Report of Session, Chicago, Sept. 20, 1940

Present at the session of the Committee on Medical Preparedness of the American Medical Association, held in Chicago, September 20, were:

Dr. James E. Paullin, Acting Chairman	Dr. Arthur W. Booth
Dr. Charles A. Dukes	Dr. Olin West
Dr. Roy W. Fouts	Dr. Morris Fishbein
Dr. John H. O'Shea	Dr. R. G. Leland
Dr. Stanley H. Osborn	Dr. E. L. Henderson
Dr. Walter G. Phippen	Dr. R. L. Sensenich
Dr. Fred W. Rankin	Dr. Thomas S. Cullen
Dr. Harvey B. Stone	Colonel Albert G. Love
Dr. Sam E. Thompson	Dr. H. H. Shoulders
	Dr. James R. Bloss

Dr. Paullin discussed the manner in which physicians would be selected for the induction boards. Dr. Fishbein indicated the necessity for having exact names for each of the various committees of the boards to be appointed. It was agreed that Medical Advisory Board would be the name adopted for the physicians appointed in the states to act as appeal boards from local draft board decisions and that the board appointed by the Army to give the physical examinations for conscripted men before entrance into military service would be known as the Medical Induction Board. It was pointed out that it was quite possible for a physician to serve on the appeal board, which is the body appointed to act as a legal board in passing on appeals from decisions of local draft boards, exactly as a physician may also be a member of a local draft board in a capacity as a citizen rather than in a medical capacity.

Colonel Love pointed out that in some instances induction boards might travel to sparsely populated areas to conduct physical examinations rather than to have the men who were conscripted sent to the center where the induction board would hold its sessions.

COMPENSATION FOR MEDICAL SERVICES

Extended discussion brought the conclusion that physicians would volunteer their services for local boards and medical advisory boards. Colonel Love explained that the specialists who would serve on induction boards would be paid as being in the military service. By vote the conference recommended that physicians volunteer their services to local and medical advisory boards. It was also voted that a subcommittee be appointed to consider the amounts and charges to be made for special

laboratory services for local and medical advisory boards in the field of radiology and clinical pathology.

Action was also taken to the effect that a two thirds vote of the committee in case of mail vote would be considered as constituting approval.

The compensation for members of medical induction boards was recommended to be that of the rank of major, with allowances.

MECHANISM OF APPOINTMENT OF MEMBERS OF INDUCTION BOARDS

The committee recommended that members of induction boards be appointed by nomination from the state chairmen to the headquarters of the Committee on Medical Preparedness, which would then supply acceptable lists to the corps area commanders. Dr. Leland presented the system of tabulation by which men acceptable in the various specialties will be listed so as to be available for this purpose.

CORRECTION OF DEFECTS IN MEN REJECTED FOR PHYSICAL REASONS

It was moved and approved that the committee recommend to the Selective Service draft boards that registrants rejected on account of physical defects be given a statement on request as to the nature of the defects for which they were rejected.

INCOME TAX

On motion and approval it was recommended to the Treasury Department that the resolution of Dr. Kopetzky with regard to income tax be approved and that the taxes on such funds be allocated either at their source or to the individual but not to both.

SEROLOGIC EXAMINATION OF REGISTRANTS

After extended discussion it was moved and approved that the committee defer any action on the question of serologic tests for registrants. It was also moved and approved that a serologic test be a part of the examinations to be made by induction boards.

THE STATUS OF NEGRO PHYSICIANS

The secretary presented a communication received from the committee representing the National Medical Association as to the status of Negro physicians in medical military preparedness and requesting membership of Negro physicians on the Committee on Medical Preparedness. The committee endorsed a reply of the Board of Trustees to the effect that the Committee on Medical Preparedness had been appointed by the House of Delegates and that it would be impossible to change the membership of that committee until a further action of the House of Delegates became possible.

INSPECTION OF SCHOOLS OF PHYSICAL THERAPY

The secretary presented a request from the Committee on Physical Therapy of the National Research Council that the Council on Medical Education and Hospitals of the American Medical Association inspect schools of physical therapy for their ability to provide physical therapy technicians and physicians specializing in physical therapy for military needs. It was moved that the communication be received and referred to the Council on Medical Education and Hospitals with approval.

PREPARATION OF WAR MANUALS

The secretary presented a communication relative to the preparation of manuals dealing with medical subjects for the use of the medical military services. This communication was referred to the Committee on Information of the National Research Council, which has these matters in hand.

OFFICIAL STATUS OF THE COMMITTEE ON MEDICAL PREPAREDNESS

After discussion it was approved that the Executive Committee of the Committee on Medical Preparedness be authorized to present to the Coordinating Committee on Medical Preparedness of the Council on National Defense the needs of the Committee on Medical Preparedness as far as concerns any budget and the establishment of suitable status for the committee in relation to the Coordinating Committee.

AMERICAN PHYSICIANS VOLUNTEERING FOR SERVICES IN THE UNITED KINGDOM

A communication was presented by the secretary from the secretary of the British embassy requesting that announcement be made to the effect that "The registration and selection of American volunteer doctors for duty in the Emergency Medical Service in the United Kingdom will in the future be undertaken by the American Hospital in Britain, Limited, 321 East Forty-Second Street, New York City. Dr. Foster Kennedy, together with an advisory board of this organization, will be in direct communication with the Ministry of Health in England concerning all these matters."

LECTURES ON MEDICAL PREPAREDNESS

The speakers for current lectures in the course on medical preparedness presented by the Philadelphia County Medical Society have been announced as follows:

Lieut. Col. Arthur P. Hitchens, Medical Corps, U. S. Army, professor of military science and tactics, Concentrations of Civilian Personnel—Epidemiologic Aspects, Contagious and Venereal Disease Problems, October 3.

Edwin W. Adams, associate superintendent of schools, Expected Psychiatric Problems in a Mobilization, October 10.

Dr. William Bates, Surgery of War as Contrasted with Industrial Surgery, and Dr. James B. Mason, Mechanism of Wound Production by Projectiles, October 17.

Station WDAS in Philadelphia is broadcasting a part of each of these lectures on Thursday afternoons.

THE BRITISH NEED SURGICAL SUPPLIES

The Medical and Surgical Supply Committee has issued an appeal to doctors to join a nationwide campaign for medical and surgical supplies to equip emergency stations and field hospitals to relieve the present medical crisis in England. The British Red Cross has cabled that it urgently requires surgical instruments of all kinds and five tons of plain lint and two tons of boric lint. The Medical and Surgical Supply Committee, which is sponsored by a group of physicians, acknowledges donations of medical supplies from several large pharmaceutic and instrument companies; also some gifts for funds from various parts of the country. The committee hopes to equip 500 emergency stations, as well as field hospitals. A first aid post can be equipped for $500. Contributions should be made out to the treasurer of the Medical and Surgical Supply Committee, Arthur Kunzinger, of the Chase National Bank. The headquarters office of the committee is at 420 Lexington Avenue, New York City.

ORGANIZATION SECTION

OFFICIAL NOTES

ADDRESSES BY OFFICIAL STAFF

DR. PAUL C. BARTON:

October 22—Southwest Missouri State Teachers College, Springfield, Mo.

October 22—Woman's Auxiliary to the Greene County Medical Society, Springfield, Mo.

DR. W. W. BAUER:

October 5—County School Teachers, La Porte, Ind.

October 6.—Health Education Institute, American Public Health Association, Detroit.

October 8—American Public Health Association, Detroit.

October 10—Northeast Lions' Club, Detroit.

October 11—Joliet Woman's Club, Joliet, Ill.

October 17—West Virginia State Nurses Association, Clarksburg.

October 27—Academy of Medicine and the Monroe County Medical Society, Rochester, N. Y.

October 29—Indiana State Medical Society, Woman's Auxiliary, French Lick, Ind.

DR. MORRIS FISHBEIN:

October 4—Medical Faculty University of Minnesota, Minneapolis.

October 7—Military Training Unit, University of Minnesota, Mayo Foundation, Rochester, Minn.

October 10—University of Nebraska, Lincoln.

October 24—Inauguration of new president, Ohio State University, Columbus.

DR. EDWIN P. JORDAN:

October 11—Will-Grundy County Medical Society, Joliet, Ill.

October 23—American College of Surgeons and American Association of Medical Record Librarians, Chicago.

DR. FRANK H. LAHEY:

October 9—Middlesex South District Medical Society, Cambridge, Mass.

October 18—Inter-State Postgraduate Assembly, Cleveland.

October 21—American College of Surgeons, Chicago.

October 30—Indiana State Medical Society, French Lick, Ind.

DR. PAUL A. TESCHNER:

October 11—Grant Hospital, Chicago.

October 14—University of Illinois, Chicago.

October 16—Methodist Church, Lombard, Ill.

October 31—Men's Bible Class, Austin Methodist Episcopal Church, Chicago.

DR. NATHAN B. VAN ETTEN:

October 7—Wayne County Medical Society, Detroit.

October 16—Inter-State Postgraduate Assembly, Cleveland.

October 20—The Cathedral at Boston.

October 22—Bronx County Medical Society, New York.

October 28—Oklahoma Medical Association, Oklahoma City.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 960, proposing to extend the classified executive civil service of the United States, has passed the Senate, with amendments. Senator Hatch, New Mexico, submitted the following amendment, which was adopted by the Senate: "In appointing, or fixing requirements with respect to the appointment of, persons to any civil position in the government service no officer or employee of any executive department, independent establishment or agency (including government-owned, government-controlled corporations) of the United States shall discriminate against any applicant or deny to any applicant the privilege of taking any competitive examination held for the purpose of determining the qualifications of applicants for such position, because such applicant (1) has not been graduated from a particular school; (2) has not been graduated from a school which has been approved or accredited, or assigned a particular rating or classification, by any association, organization, or group; or (3) is not a member of any professional, technical, or other society or association." This bill will be further considered by a conference committee, composed of conferees on the part of the House and Senate. The Hatch amendment, if it remains in the bill, will open the way for the appointment of graduates of unapproved medical schools to any civil position in the government service. H. R. 6450 has been reported to the Senate, proposing to establish certain rights for combat veterans of wars of the United States. The bill provides, in part, that where a veteran is shown to have been engaged in combat with an enemy of the United States, or during service in some war, campaign or expedition, to have been subjected to other arduous conditions of military or naval service, such disability as can reasonably be considered to have been due to or aggravated by the conditions of all of his active military or naval service shall be determined to be directly due to or aggravated by such service in line of duty, unless the contrary is shown by clear and unmistakable evidence. S. 4224 has passed the Senate, providing that in time of war or during an emergency declared by the President or by Congress the Secretary of War may, in his discretion, dispense with any of the examinations for promotion in the Regular Army of officers of the Medical, Dental and Veterinary Corps, except those relating to physical examinations.

Bill Introduced.—S. 4371, introduced by Senator Schwellenbach, Washington, proposes that the United States Public Health Service shall provide for the care and relief of sick and disabled persons (1) employed on board any registered, enrolled or licensed vessel of the United States in the performance of duties of a workshop character or (2) employed or engaged in commercial fishing on board any such vessel or on board any boat operating from any such vessel as a base.

DISTRICT OF COLUMBIA

Bill Introduced.—S. 4376, introduced by Senator Byrd, Virginia, provides that, notwithstanding any limitation relating to the time within which an application for a license must be filed, the Commission on Licensure to Practice the Healing Art in the District of Columbia is directed to issue a license to practice chiropractic to Lou Davis on condition that he shall be found by the commission to be otherwise qualified to practice under the provisions of the healing arts practice act.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Plague Infection. — According to *Public Health Reports*, plague infection was proved in a pool of 129 fleas from fifteen ground squirrels (C. fisheri) submitted to the laboratory on July 15 from Arrowhead Dump, 1 mile east of Lake Arrowhead, San Bernardino County.

Society News.—The Los Angeles Society of Ophthalmology and Otolaryngology was addressed, September 23, by Drs. George L. Kilgore, San Diego, on "Repair of Corneal Scar"; John N. N. Osburn, Los Angeles, "Fifteen Years' Experience with Intra-Ocular Foreign Bodies," and Lieut. Thomas L. Allman, U. S. Navy, "Physical Requirements for Naval Aviation."——The Los Angeles Cancer Society was addressed, September 30, by Drs. Robert S. Stone and John H. Lawrence, San Francisco, on "Neutrons in the Treatment of Cancer" and "Artificial Radioactive Substances in Relation to Clinical Medicine," respectively. Paul C. Aebersold, Berkeley, spoke on "Modern Nuclear Physics and Cancer Therapy."——Dr. Robert E. Wyers presented a "Study of 260 Cases of Mongolism with Special Reference to Congenital Heart Lesions" before the Los Angeles Society of Neurology and Psychiatry, September 18, and Dr. David L. Reeves, "Amyotonia Congenita of Oppenheim: Report of Case with Autopsy."——Dr. Karl A. Menninger, Topeka, Kan., discussed "Eve and the Flying Dutchman: A Psychiatric Study of a Certain Aspect of the Relations Between Men and Women" before the Hollywood Academy of Medicine, September 12.

DISTRICT OF COLUMBIA

Annual Scientific Assembly.—The Medical Society of the District of Columbia will conduct its annual scientific assembly at the Mayflower Hotel, Washington, October 15-17, selecting for the theme this year cardiovascular renal diseases. The following doctors will speak:

Richard Schatzki, Boston, Roentgen Diagnosis in Cardiovascular Disease.
Raymond Hussey, Baltimore, Some Interesting Electrocardiographic Interpretations.
Helen B. Taussig, Baltimore, Congenital Heart Disease.
Thomas Duckett Jones, Boston, Acute Rheumatic Carditis.
Harry H. Donnally, Washington, Management of the Child with Inactive Rheumatic Heart Disease.
Edward F. Bland, Boston, Differential Diagnosis of Congenital and Rheumatic Heart Disease in Children.
Walter A. Bloedorn, Washington, Recognition and Treatment of the Various Forms of Pericarditis.
Wallace M. Yater, Washington, Diseases of the Aorta.
Isaac Alexander Bigger, Richmond, Va., Diagnosis and Treatment of Heart Wounds.
George Louis Weller Jr., Washington, Surgical Shock and Circulatory Failure.
Thomas S. Lee, Washington, Hypertensive Heart Disease.
William Thornwall Davis, Washington, Changes in the Fundus Oculi in Cardiovascular Disease.
Edward Weiss, Philadelphia, Renal Involvement in Hypertensive Vascular Disease.
Maurice Charles Pincoffs, Baltimore, Cardiac Aspects of Chronic Nephritis.
Joseph Earle Moore, Baltimore, Cardiovascular Syphilis.
Howard B. Sprague, Boston, Clinical and Electrocardiographic Findings in the Aging Heart.
James Edwin Wood Jr., Charlottesville, Va., Diagnosis and Treatment of Cardiac Arrhythmias.
James Alexander Lyon, Washington, Failure of the Left and Right Sides of the Heart.
Harry Gold, New York, Digitalis: Its Action and Usage.
Ralph M. LeComte, Washington, Cardiovascular Complications of Prostatic Obstruction.
Joseph B. Wolffe, Philadelphia, Recognition and Management of Cardiac Neurosis.
Harold M. Marvin, New Haven, Conn., Diagnostic Criteria of Coronary Artery Disease.
Edwin Cowles Andrus, Baltimore, Acute Coronary Thrombosis.
Arthur M. Master, New York, Role of Effort, Trauma, Work and Occupation in the Onset and Subsequent Course of Coronary Occlusion.
Irving Sherwood Wright, New York, Diagnosis and Conservative Treatment of Peripheral Vascular Diseases.
Norman E. Freeman, Philadelphia, Surgical Treatment of Peripheral Vascular Disease.
Achilles L. Tynes, captain, medical corps, U. S. Army, The Heart During Anesthesia.

The program also includes a hobby show and luncheons to be addressed by Major Gen. James C. Magee, surgeon general of the U. S. Army, and Edward M. Curran, U. S. Attorney for the District of Columbia. There will be a public meeting Wednesday evening.

GEORGIA

Society News.—The Fulton County Medical Society was addressed in Atlanta, September 19, by Drs. Hulett H. Askew and Rufus A. Askew on "Hemorrhoidectomy." Dr. Cyrus W. Strickler Jr. gave a clinical talk on "Intravenous Sodium Sulfapyridine Monohydrate in Pneumonia." The society was addressed, September 5, among others, by Drs. William R. Crowe Jr. and Gene Nardin, Atlanta, on "Hyperparathyroidism."

Annual Industrial Meeting.—The third annual meeting of Georgia Association of Industrial Surgeons was held at the Ansley Hotel, Atlanta, September 25. Among the speakers were:

Dr. McIver Woody, New York, Industrial Medicine as a Specialty.
Dr. Lloyd Noland, Birmingham, Ala., subject not announced.
Drs. Edward C. Holmblad and Kenneth L. Matson, Chicago, Gas Gangrene, Plea for Better Prophylaxis.
Dr. Cleveland D. Whelchel, Gainesville, Chest Surgery.
Dr. Benjamin H. Minchew, Waycross, Eye Injuries in Industry.
Dr. Samuel F. Rosen, Savannah, Occupational Dermatoses.
Dr. W. Whatley Battey, Augusta, Herniae.
Dr. Frank K. Boland, Atlanta, History of Fractures.

ILLINOIS

Physicians Honored. — Drs. Eugene D. Bergeron and Aaron S. Eshbaugh, both of Kankakee, were honored at a meeting of the Kankakee County Medical Society, September 10, marking their completion of fifty years in the practice of medicine. Both physicians were accorded special recognition for service to their community and given certificates and pins from the Illinois State Medical Society. Dr. Bergeron graduated at Chicago Medical College, now Northwestern University Medical School, in 1881. Dr. Eshbaugh graduated at Hahnemann Medical College and Hospital, Chicago, in 1886. Both have been practicing in Kankakee for about forty years.

Chicago

Annual Prize of Surgical Society.—Manuscripts for the third award of the annual prize of $250 of the Chicago Surgical Society should be submitted to the secretary not later than March 1, 1941. The prize is awarded to a young man devoting himself to surgery in Chicago, who is not a member of the Chicago Surgical Society, for meritorious work in one or both of the fields of experimental and clinical surgery. Certain qualifications must be met in the judging of the papers. Additional information may be obtained from the secretary, Dr. Michael L. Mason.

KENTUCKY

Society News. — Dr. Robert Julian Estill, Lexington, addressed the Woodford County Medical Society, Versailles, September 6, on "Diseases of the Newborn."——Dr. William B. Moore addressed the Harrison County Medical Society, Cynthiana, September 2, on "Treatment of the Failing Heart."

State Medical Election.—Dr. Elmer L. Henderson, Louisville, was named president-elect of the Kentucky State Medical Association at the annual meeting in Lexington in September, and Dr. Austin Bell, Hopkinsville, became president. Vice presidents elected were Drs. William R. Parks, Harlan; Ernest Lee Heflin, Louisville, and William E. Gary, Hopkinsville. The 1941 meeting will be in Louisville.

Personal.—Dr. Andrew B. Steele has resigned as clinical director of the Western State Hospital, Hopkinsville, to join the staff of the Indiana state welfare department, it is reported. ——Dr. William G. Morgan, Cadiz, health officer of Trigg and Lyon counties, has been appointed health officer of Daviess County, with headquarters in Owensboro. He succeeds Dr. William Lee Tyler Jr., who has been part time health officer. ——Dr. Jerauld A. Campbell, Niagara Falls, N. Y., has been appointed health officer of Grayson County.——Dr. Mildred E. Burton, Berea, has been appointed health officer of Owsley County.

LOUISIANA

Dr. Musser Named President of State Board of Health.—Dr. John H. Musser, professor of medicine at Tulane University of Louisiana School of Medicine, New Orleans, has been appointed president of the Louisiana State Board of Health to serve on a part time basis until January during the reorganization of the board. Dr. Musser succeeds Dr. Joseph A. O'Hara, who resigned after holding the position since 1928. The change was to be effective September 1, newspapers reported. The appointment of Dr. Robert H. Onstott, U. S. Public Health Service, as executive officer of the board was also announced. In this capacity, on a full time basis, he will act as medical consultant in the reorganization of the board.

MICHIGAN

The Business Side of Medicine.—A symposium on the business side of medicine was a feature of the seventy-fifth annual meeting of the Michigan State Medical Society, Detroit, September 24. It was arranged especially for the secretaries and office assistants of members of the state society with Dr. Allan W. McDonald, Detroit, president, Wayne County Medical Society, presiding. Dr. Paul R. Urmston, Bay City, then president-elect of the state society, gave an address of welcome. Other speakers included:

Mrs. Marjorie Euler, Topeka, Kan., The Highlights of Twenty-Five Years of Service.
Miss Maxine Robinson, Muskegon, Organizing the Medical Assistants' Society of Muskegon County.
J. D. Laux, executive director, Michigan Medical Service, Detroit, How to Bill Michigan Medical Service.
Dwight Anderson, LL.B., New York, director, public relations bureau, Medical Society of the State of New York, What Every Woman Knows.

Postgraduate Programs.—A series of postgraduate courses for practicing physicians will soon begin throughout Michigan under the auspices of the Michigan State Medical Society, University of Michigan Medical School, Ann Arbor; Wayne University College of Medicine, Detroit, and the state department of health, Lansing. The programs will be conducted at the following places:

Ann Arbor, October 10, 17, 24, 31.
Battle Creek-Kalamazoo, jointly, October 8, 15, 22, 29.
Flint, October 9, 16, 23, 30.
Grand Rapids, October 10, 17, 24, 31.
Lansing-Jackson, jointly, October 10, 17, 24, 31.
Manistee-Traverse City-Cadillac-Petoskey, jointly, October 11, 18, 25, November 1.
Mount Clemens, October 9, 16, 23, 30.
Saginaw, October 7, 14, 21, 28.

Included among the subjects for discussion are: the newborn period; the management of labor; development of hernia; significance of albuminuria; the psychoneuroses; laboratory procedures for office practice; nasal accessory sinus diseases in the practice of medicine, and the differential diagnosis of coma.

MINNESOTA

Changes in the Medical School.—New appointments to the University of Minnesota Medical School, Minneapolis, included the following:

Lemen J. Wells, Ph.D., assistant professor of anatomy, University of Missouri School of Medicine, Columbia, as associate professor of anatomy.
Dr. Charlotte M. Gast, formerly of New Bedford, Mass., assistant professor and assistant director of a course in medical technology.
Edwin S. Fetcher Jr., Ph.D., Chicago, and Robert B. Dean, Ph.D., Rochester, N. Y., instructors in the department of physiology.

The following promotions in the medical school have also been announced:

Halvor O. Halvorson, Ph.D., professor of bacteriology.
Dr. Raymond N. Bieter, professor of pharmacology.
Dr. William A. O'Brien, professor of preventive medicine and public health and director of postgraduate medical education.
Dr. Cecil J. Watson, professor of medicine and director of the division of internal medicine.
Dr. William T. Peyton, professor of surgery and director, division of neurosurgery.
George O. Burr, Ph.D., professor of plant physiology, has in addition been appointed director of the division of physiologic chemistry.
Dr. Arthur C. Kerkhof, clinical associate professor of medicine.
Dr. Starke Hathaway, clinical psychologist and associate professor of nervous and mental diseases.
Dr. James B. Carey, clinical associate professor of medicine.
Wallace D. Armstrong, Ph.D., associate professor of physiology and director of biological research in dentistry.

NEVADA

State Medical Meeting at Las Vegas.—The thirty-seventh annual meeting of the Nevada State Medical Association will be held at Las Vegas, October 10-12, with headquarters at the Elks Club. The scientific program will include the following speakers:

Dr. Victor S. Randolph, Phoenix, Ariz., Surgical Treatment of Pulmonary Tuberculosis.
Dr. Louis E. Viko, Salt Lake City, Etiology and Treatment of Hypertension.
Dr. William Whitfield Crane, Oakland, Calif., Surgical Treatment of Hypertension.
Dr. Verne C. Hunt, Los Angeles, Surgical Management of Carcinoma of the Colon.
Dr. Kenneth S. Davis, Los Angeles, Limitation and Evaluation of the X-Ray in the Diagnosis of Disease of the Gallbladder.
Dr. Gerald Brown O'Connor, San Francisco, Immediate Management of Surface Injuries.
Dr. Roland W. Stahr, Reno, Practical Points in Pediatrics.
Dr. John C. Wilson, Los Angeles, Present Status of Treatment of Fractures of the Neck of the Femur.
Dr. Hugh T. Jones, Los Angeles, Problems Encountered in the Orthopedic Care of the Knee Joint.
Dr. A. Elmer Belt, Los Angeles, Obstructive Uropathy in Childhood.

NEW HAMPSHIRE

Dr. Lancaster Goes to Dartmouth.—Dr. Walter B. Lancaster, for many years ophthalmic surgeon at the Boston City Hospital and the Massachusetts Eye and Ear Infirmary and a member of the faculty of Harvard Medical School, Boston, has been appointed chief of staff of the Dartmouth Eye Institute at Dartmouth College, Hanover, effective November 1. Dr. Lancaster is at present lecturer in ophthalmology on the staff of the Courses for Graduates at Harvard and consulting ophthalmic surgeon at the New England Hospital for Women and Children. He is a former president of the American Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology, the New England Ophthalmological Society and the American Board of Ophthalmology and in addition holds memberships in various other scientific societies. In 1928 he was chairman of the section on ophthalmology of the American Medical Association. He was also chairman of the section on ophthalmology of the National Conference on Nomenclature of Disease. During the World War he was head of the department of ophthalmology in the aeronautical research laboratories at Mitchel Field, New York. He graduated from Harvard Medical School in 1889.

NEW YORK

Million Volt X-Ray Unit at Buffalo.—Installation of a million volt x-ray therapy unit at the State Institute for the Study of Malignant Disease, Buffalo, was recently announced. A new three story wing has been built at the institute to accommodate the new unit, the offices of the director and other business offices and in addition it provides seventy-eight beds. Memorial Hospital, New York, and St. John's Hospital, Cleveland, have similar installations. Unlike previous x-ray equipment, this weighs only about 4,000 pounds and occupies only a single room.

Personal.—Dr. Harry Beckett Lang, Brentwood, has been appointed superintendent of the Buffalo State Hospital, succeeding Dr. John A. Pritchard, who has been appointed superintendent of the St. Lawrence State Hospital, Ogdensburg. ——The Wayne County Medical Society at its August meeting honored Dr. John F. Myers, Sodus, for his long years of practice. Dr. Myers graduated from Columbia University College of Physicians and Surgeons and has been a member of the Wayne County society for fifty years. He received a set of travel books as a memento.

New York City

Railway Surgeons' Meeting.—The seventeenth annual meeting of the Association of Surgeons of the New York Central System was held at the Hotel Biltmore, September 24-26. Among the speakers were Drs. William W. Herrick, on "Prognostic Factors in Circulatory Disease"; Charles Gordon Heyd, "A Consideration of Mortality in Gallbladder Disease," and Kristian G. Hansson, "Indications and Limitations of Physiotherapy in Railroad Injuries."

Hospital News.—The cornerstone of a new million dollar five-story dispensary building at Kings County Hospital, Brooklyn, was laid September 25. Speakers at the ceremony included Mayor La Guardia, Drs. Walter A. Coakley, president of the medical board, and Emanuel Giddings, medical superintendent. This will be the third of a series of ten dispensaries planned by the department of hospitals for different sections of the city to relieve overcrowding and inadequate service at the city's hospitals. It was reported by the hospital department that clinic visits at Kings County Hospital had increased from 163,638 in 1933 to 358,072 in 1939. New dispensaries were opened at Greenpoint Hospital, Brooklyn, in 1937 and on Welfare Island August 1 of this year.

OHIO

Society News.—Dr. Charles T. Way, Cleveland, addressed the Portage County Medical Society, Kent, September 5, on diseases of the kidney.——Dr. Gilson C. Engel, Philadelphia, addressed the Stark County Medical Society, Canton, September 11, on "Diagnosis of Intra-Abdominal Conditions."

Professor Waite Retires.—Frederick C. Waite, Ph.D., professor of histology and embryology at Western Reserve University School of Medicine since 1906 and in the dental school since 1915, has retired, having reached the age of 70. Dr. Waite took his undergraduate work and a master's degree at Western Reserve and his doctorate at Harvard University in 1898. He was appointed to the faculty of Western Reserve in 1901 as assistant professor of histology and embryology. The teaching of histology and embryology has now been made an integral part of the department of anatomy under the direc-

tion of Dr. Normand L. Hoerr. Samuel W. Chase, Ph.D., will continue the teaching of dental histology; he has had charge of this course for several years.

PENNSYLVANIA

Society News.—Dr. Garfield G. Duncan, Philadelphia, will present a "Practical Discussion of Diabetes for the General Practitioner" before the Dauphin County Medical Society, Harrisburg, October 8.

Philadelphia

Lectures at the College of Physicians.—The College of Physicians of Philadelphia opened its 1940-1941 series of scientific lectures, September 25, with an address by Dr. George W. Corner, Baltimore, on "Physiological Basis of Corpus Luteum Therapy," the Nathan Lewis Hatfield Lecture. Dr. John F. Fulton, New Haven, Conn., will deliver the S. Weir Mitchell Oration, November 6, on "Neurology and War," and Dr. Allen O. Whipple, New York, the Thomas Dent Mütter Lecture, December 4, on "Recent Studies in the Circulation of the Portal Bed and of the Spleen in Relation to Splenomegaly." Three lectures for the public have been arranged as follows:

Dr. Chevalier Jackson, The Bronchoscope, November 15.
Dr. Hubley R. Owen, Activities of the Department of Public Health, with Plans for the Future, Jan. 24, 1941.
Dr. Richard A. Kern, Allergy and You, April 18, 1941.

Pittsburgh

Society News.—At the first fall meeting of the Allegheny County Medical Society, September 17, the speakers were Drs. Clifford Lee Wilmoth on "Abscess in and About the Liver"; Paul Gross, Franklin B. Cooper and Alfred F. Knoll, "Progress in Chemotherapy"; Louis H. Landay, "Treating the Allergic Patient," and William Shapera, "Dilantin Therapy in Certain Nervous Disorders."

TEXAS

Society News.—The fall meeting of the Texas Surgical Society will be held at the Rice Hotel, Houston, October 7-8, with Drs. Alfred W. Adson, Rochester, Minn., and Maxwell Harbin, Cleveland, as guest speakers.——Drs. James W. Ward and William P. Phillips, Greenville, addressed the Hunt-Rockwall-Rains County Medical Society, Greenville, September 10, on diseases of the eye and surgical treatment of acute diseases of the abdomen, respectively.——At a meeting of the Dallas County Medical Society, September 12, the speakers were Drs. Charles A. Ault Jr. on "Sarcoma of the Heart"; Elizabeth C. Williams, "Orthoptics as Related to General Medicine," and Donald G. Kilgore, "Coccydynia."

District Meeting in Texarkana.—The Northeast Texas District Medical Society will meet in Texarkana, October 8. Among the speakers will be:

Dr. Joseph F. McVeigh, Fort Worth, Some Observations on Malaria and Its Treatment.
Dr. Calvin R. Hannah, Dallas, Early Diagnosis of Pregnancy.
Dr. Walter G. Reddick, Dallas, The Use of Sulfanilamide Derivatives in Acute Infections.
Dr. Robert K. Womack, Longview, Practical Points in the Treatment of Gonorrhea in the Male.

Dr. Holman Taylor, Fort Worth, secretary of the State Medical Association of Texas, addressed a luncheon meeting on "Medical Preparedness" and Dr. Preston Hunt, Texarkana, president of the state association, also delivered an address.

VERMONT

State Medical Meeting in Rutland.—The one hundred and twenty-sixth annual meeting of the Vermont State Medical Society will be held at the Hotel Berwick, Rutland, October 10-11, under the presidency of Dr. Clarence F. Ball, Rutland. The following members of the faculty of the University of Rochester School of Medicine and Dentistry, Rochester, N. Y., will be the guest speakers:

Dr. Charles M. Carpenter, Diagnosis and Control of Gonococcal Infections.
Dr. Samuel W. Clausen, The Importance of Congenital Obstructions of the Intestines as a Cause of Vomiting in Infancy.
Dr. William S. McCann, Practical Considerations of the Newer Physiologic Studies of Renal Disease.
Dr. Stafford L. Warren, Survey of the Newer Aspects of Radiographic Diagnoses in Relation to the General Practitioner.
Dr. Winfield W. Scott, Hematuria.
Dr. Karl M. Wilson, The Use of X-Rays as a Diagnostic Aid in Obstetrics and Gynecology.
Dr. William L. Bradford, Active and Passive Immunity Against the Common Infectious Diseases.
Dr. William J. Merle Scott, Some Problems in Gastric Surgery.

Dr. Ball will deliver his presidential address on "Medical Vision"; Dr. Wilmer W. Angell, Randolph, the vice presidential address on "The Challenge of the Small Hospital," and Dr. Hardy A. Kemp, dean and professor of bacteriology and preventive medicine, University of Vermont School of Medicine, Burlington, will speak on "Plans for Postgraduate Medical Education in Vermont."

A special program of ophthalmology and otolaryngology has been arranged with the following speakers:

Dr. David Harold Walker, Boston, Practical Consideration of Ear Diseases.
Dr. Deforest C. Jarvis, Barre, Twelve Varieties of the Common Cold.
Dr. Walter B. Lancaster, Boston, Difficulties Encountered in Measuring Errors of Refraction.

There will also be a special meeting on pathology and radiology at which cases of cancer of the stomach will be presented, and Dr. Robert J. Stein, Newport, will read a paper on "Stromal and Systemic Changes in Carcinoma of the Breast."

The Vermont regional committee on fractures of the American College of Surgeons will present a symposium with the following speakers: Drs. Henry C. Marble, Boston, "Compound Fractures"; Andrew William Reggio, Boston, "Important Points in the Treatment of Ankle-Joint Fractures," and Otto J. Hermann, Boston, "Injuries to the Wrist and Foot."

WYOMING

Plague Infection.—According to *Public Health Reports*, plague infection has been proved in a pool of fifty-four fleas from twenty-two ground squirrels, in tissue from one ground squirrel, all from a locality from 8 to 10 miles north of Kendal Ranger Station, Sublette County, Wyo., and in a pool of eighteen fleas from fourteen ground squirrels taken from 12 to 15 miles north of the same station. The ground squirrels, all of the same species, C. armatus, were all shot the same day, August 6.

GENERAL

Regional Meeting of Obstetricians and Gynecologists.—The twelfth annual meeting of the Central Association of Obstetricians and Gynecologists will be held in Indianapolis, October 10-12, at the Hotel Lincoln, under the presidency of Dr. Jennings C. Litzenberg, Minneapolis. Dr. Robert Otto Meyer, Minneapolis, will be the guest speaker on "Some Aspects of the Pathology of Hydatidiform Mole and Chorionepithelioma." Among other speakers will be:

Drs. Carl P. Huber and Jack C. Shrader, Indianapolis, Blood Prothrombin Levels in the Newborn (the clinical prize award essay).
Dr. Harold Henderson, Detroit, The Relative Effect of General and Local Anesthesia on Asphyxia Neonatorum.
Dr. John R. Wolff, Chicago, The Leukocyte Count in Labor.
Drs. Harry L. Stewart Jr. and Jean P. Pratt, Detroit, Inhibition of Lactation.
Dr. Philips J. Carter, New Orleans, Conglutinatio Orificii Externi as a Factor in Delayed Labor.

Infantile Paralysis Fund Raised on President's Birthday.—The Committee for the Celebration of the President's Birthday reported to President Roosevelt, September 24, that the 1940 "Fight Infantile Paralysis Campaign" raised a net total of $1,407,245.74. Of the total net proceeds, $768,780.29 remained in the communities and chapters of the National Foundation for Infantile Paralysis throughout the county. The foundation received $638,465.45 to carry on its work aimed toward eradicating and controlling the disease. The major part of the fund was raised by the parties and dances held on the President's birthday, January 30, and by sports events promoted by the "March of Sports." The "March of Dimes" raised a net total of $250,205.07. California led the states in the net total raised, $209,042.26; New York was second with $199,258.38, and Pennsylvania third with $86,644.67. The foundation's work is carried on through grants issued to universities, colleges and hospitals for research; it aids hospitals and institutions in the treatment of after-effects of the disease, distributing information on diagnosis and treatment and on the use of iron lungs, splints and braces. It sends doctors, nurses, epidemiologists, respirators and splints into towns and cities where they are needed. The chapters are working with health authorities and physicians in epidemic regions, using chapter funds to see that no case is neglected, according to the committee's report. The total number of cases this year exceeds the total for the same period last year, the principal outbreaks being in Washington, West Virginia, Indiana, Ohio, Michigan, Iowa, Kansas, Illinois, Kentucky and Montana. The number up to September 7, according to figures compiled by the U. S. Public Health Service, was 4,037, compared with 3,454 for the same period in 1939. Mr. Basil O'Connor, New York, is president of the National Foundation for Infantile Paralysis and Mr. Keith Morgan, New York, is national chairman of the Committee for the Celebration of the President's Birthday.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 24, 1940.

Examination of the Recruit's Heart

A committee appointed by the government, under the chairmanship of Lord Horder, to advise on the examination of recruits has presented recommendations on the methods of detecting "the effort syndrome" and diseases of the heart and arteries. The committee has submitted recommendations which amend and amplify the instructions existing for the guidance of medical boards. The committee was assisted in its work by the Cardiac Society of Great Britain and Ireland and by Sir Thomas Lewis and Dr. Paul Wood. "Effort syndrome" is defined as a condition in which the characteristic symptoms are nervousness, a feeling of exhaustion, left mammary discomfort, palpitation, giddiness and dyspnea on exertion. Many men break down during training or on active service with these symptoms. The great majority of them are neuropathic but in a small group the symptoms are attributable to chronic or temporary toxemia. The condition is rarely an expression of any disorder of the heart. A board may be able to foretell that certain recruits, by their appearance and demeanor and by evidence of nervous instability, are likely to break down in this way. Habitual avoidance of exertion in recreation is particularly suggestive. An exercise tolerance test affords little guidance in detecting potential sufferers from this syndrome but may be valuable in gaging the degree of emotional disturbance when the characteristic symptoms are already manifest.

The following revised form of tolerance test is now prescribed. 1. The pulse rate is taken for fifteen seconds with the man standing. 2. The man places one foot on a chair at least 15 inches high. He then raises himself until both feet are on the chair and the body is upright. He then lowers himself until one foot is on the floor. This is repeated twenty times in sixty seconds. The pulse is then taken for fifteen seconds. 3. The man stands still, and forty-five seconds later the pulse is taken for fifteen seconds. It should then be the same as or lower than the original rate. The persistence of any dyspnea or distress should be noted. If the original pulse rate is regained in sixty seconds and there is no dyspnea or distress he may be regarded as having good exercise tolerance. If the response is unsatisfactory the cause may be nervous instability or some cardiovascular defect and must be investigated. The test alone does not afford conclusive evidence of these conditions or of the man's unfitness for grade 1. The test may be rendered misleading by temporary factors such as a common cold or lack of fitness following prolonged sedentary work.

The heart should always be examined while the man is standing and also while he is lying on his left side; otherwise heart murmurs are difficult to detect. They should be listened for on both sides of the sternum and while the breath is held in full expiration. A man should be classed as in grade 4 whose heart shows signs of enlargement, aortic or mitral disease or congenital heart disease, even though well compensated and the existence of a fair response to the exercise tolerance test. A systolic murmur heard at the apex is not to be accepted alone as evidence of organic disease, but high grade exercise tolerance should be required and mitral or aortic disease carefully excluded. If the systolic bruit is slight and the only sign, the man may be accepted as of grade 1 provided he has good exercise tolerance. A systolic murmur at the base is common in health and may be disregarded when loudest in the pulmonary area, unless associated with other signs of congenital heart disease. If loudest in the aortic area, transmitted upward and accompanied by a thrill, it indicates aortic stenosis. If the cardiac impulse is felt beyond the midclavicular line, the heart is enlarged provided the displacement is not due to scoliosis or to pulmonary disease. The commonest causes of enlargement are aortic and mitral disease; less common causes are hypertension and congenital heart disease. Abnormal rhythm is not necessarily evidence of organic disease. Before grading, the previous history (occupation, athletic habit and other activities) must be reviewed as well as the exercise tolerance test. Tachycardia is most often an expression of nervousness, but if paroxysmal requires a low grading. Hyperthyroidism should be excluded. Cases of arrhythmia and tachycardia of doubtful nature should be referred to a consultant. In all men over 40 and in any case of cardiac enlargement or of suspected arteriosclerosis the blood pressure should be taken.

The Medical Women's Federation and the Prevention of Venereal Disease

The Medical Women's Federation has taken a strong interest in the problem of venereal disease. It has issued a statement pointing out that the large numbers of men and women in the fighting forces render the prevention of venereal disease important. The most effective way would be welfare services available to all. These would provide not only ample arrangements for healthy recreation but also education and advice in matters of health. The work of welfare officers has already proved valuable in maintaining good morale, but the staff should be augmented by suitably qualified men and women, and individual private hospitality should be welcomed in association with the official organization. Provision of this kind is of primary importance in the prevention of venereal disease.

The federation emphasizes the importance of sex teaching with the object of developing a social conscience in men and women. Education in sex hygiene should be given to all members of the fighting forces, both men and women. For women this should be given by medical women who have special experience in social hygiene. Members of the women's forces who contract venereal disease should not necessarily be dismissed but given adequate and sympathetic treatment. They should have facilities similar to those of men and have access to medical women. The federation emphasizes its belief that *maisons tolérées* are a danger to health and likely to increase venereal disease. Further, although some individual infection may be prevented by the use of "prophylactic packets," their routine distribution, by implying official sanction of illicit intercourse, tends to increase promiscuity and the incidence of venereal disease. Welfare facilities, education and treatment should also be fully available for munition workers, especially those working for long hours.

ITALY

(From Our Regular Correspondent)

Aug. 3, 1940.

Medical Aid at the Battle Front

Prof. Filippo Ferraro, who was chief of sanitation of a division of volunteers in the Spanish civil war, recently discussed in Genoa modern medical units in mobile warfare. The new ideas in military tactics and in the use of weapons necessarily have changed also the operation of the divisional medical service. Medical units in war can no longer be considered relatively stationary; on the contrary, they must meet the needs of rapid shifts of position, intensified by aerial warfare, and must follow troops in action to within the nearest distance possible. They must maintain medical equipment at all times at the highest efficiency. Basing his observations on the statistics gathered during the battles of Guadalajara and Santander, regarded by military experts as two of the most typical modern battles, the speaker pointed out that the proportion of divisional losses sustained was, on the average, 8 per cent as

compared with a 20 per cent loss recorded for the war of 1914-1918. The index for seriously wounded was about 9.5 per cent. In comparison with Italian statistics for the World War indicating 39.1 per cent as wounded by small arms and 19.5 per cent by artillery, present statistics indicate 69.3 per cent as wounded by small arms and 19.5 per cent by artillery. Seven and eight tenths per cent were wounded by bombs discharged from airplanes and 7.8 per cent by explosion of mines. As to the site of traumatic lesions, important from the point of view both of medical technic and of the handling of the wounded in the field, there was a relative increase in wounds of the lower extremities, compared with the statistics for the war of 1914-1918. The percentage for wounds of the abdomen and thorax remained practically unchanged. Mortality on the battlefield amounted to 15.7 per cent. This is in accord with the general average accepted by military medical statistics. Deaths due to freezing and gassing were few. Military physicians, he said, were not all in accord in regard to specialized surgical service. Experience had taught him that the principal function of what is referred to as the "surgical nucleus" was early intervention for all wounded promising recovery. In fact, Ferraro's statistics indicated that the shorter the distance of the "surgical nucleus" from the battle line the lower the mortality rate among the wounded and even among those operated on. Since establishing a position and getting ready required time, he favored the idea that the "nucleus" be attached either to a less advanced unit of the medical service or to an advanced field hospital. However, a more practical suggestion would be to divide the "nucleus" into two parts so as to guarantee continuity of service on the relay plan. The divisional medical staff might also request to have placed at its disposal reserve groups of surgeons to meet the need of excessive demands occurring on the same day.

Changes in the Volume of Circulating Blood

Professor Bertola discussed before the society of physicians and surgeons of Pavia the modifications which the volume of circulating blood may undergo in response to certain factors. Modifications may be caused by changes in the position of the subject during the action of certain drugs on the vegetative nervous system. In the change from a recumbent to a standing position, increases as well as decreases of the circulating blood were observed. The increases were accompanied on the whole by a lowering of the arterial blood pressure, whereas an increase in pressor levels accompanied the diminution of the circulating blood.

During the action of atropine, in general, hypovolemia prevailed in subjects in the standing position combined with hypotensive reactions and a diminution of pulse frequency. The opposite behavior was noted during the action of pilocarpine. Ergotamine showed a behavior analogous to that induced by atropine, whereas epinephrine generally increased the circulation of the blood when subjects stood and showed an increase in the pressor levels and pulse frequency. In short, substances which stimulated the vagus and the sympathetic nerve produced predominantly hypervolemia in the standing position, whereas those with inhibitory action showed a contrary behavior.

Investigations into the modifications of the volume of circulating blood and of other factors during digestion both in normal subjects and in patients with gastric disorders showed regularly an increase in the volume of circulating blood after the administration of carbohydrates, proteins, fats, salts or a mixed diet. In patients with ulcers, on the contrary, a decrease in the volume of the circulating blood was regularly observed. These results may be explained by the fact, he said, that certain organs may be regarded as filled with blood owing to the regulator function of the vegetative nervous system.

Studies of the regulatory effect of the carotid sinus on the behavior of the circulating blood when the subject changed from a recumbent position to one with the head down prevailingly indicated in normal and hypotensive persons a decrease in the circulating blood, which at times was considerable, together with an increase in the rate of circulation. In hypertensive persons, on the other hand, there were pronounced variations in the volume of the circulating blood, generally in the direction of increases. Present knowledge cannot satisfactorily explain the factors that produce these differences. However, Ferraro stressed certain facts such as the opposite behavior of pulse reaction, of arterial pressure and of the volume of circulating blood, which is typical for hypertensive persons and rare in normal and hypotensive subjects. The importance of the action of organs which act as depositories of blood and which are prevailingly regulated by the vagus and the sympathetic nerve is not overlooked. Yet the possibility is not excluded that reflex vasomotor modifications under the influence of the vasoreceptor zones may interfere with the regulation of the circulating blood.

Deaths

Prof. Luigi Sestini, physician general of the navy and a war invalid, died at Spezia. He was highly esteemed. Among the positions of responsibility held by him was the directorship of the School of Health in Naples. His special interest lay in promoting health in the navy by the institution of sanitary improvements on war vessels and by combating tuberculosis.

Marriages

WILLIAM KENNETH MASSEY, Ashcroft, B. C., Canada, to Miss Corinne Kearfoot Saunders of Winnipeg, Man., recently.

BRIAN DESMOND BEST, Winnipeg, Man., Canada, to Miss Jean Margaret Prior of Portage La Prairie, June 29.

JAMES ROY BREED, Wappingers Falls, N. Y., to Miss Jocelyn Harrington of Poughkeepsie, September 7.

JAMES PORTER LEATHERS, Nashville, Tenn., to Miss Katheryne Bowden McClain of Lebanon in August.

WILL HARDEE LASSITER JR., Selma, N. C., to Miss Kathleen Anderson of Winston Salem in August.

EMANUEL BARNETT HECHT, Ancon, Canal Zone, to Miss Adele Weinstock of New York, July 25.

ROBERT T. MCMAHON, Albany, Calif., to Miss June Huml of Oakland, July 13, in Carson City, Nev.

EILIF CARL HANSSEN, New York, to Miss Carroll Ellicott Henderson at Los Angeles, June 21.

CLAUDE FREDERICK OTTEN, Morristown, N. J., to Miss Lois Heuse of Dallas, Texas, August 17.

ROBERT WOOLFORD, Hamilton, Ohio, to Miss Mary Margaret Kilgore in Columbus, September 1.

WILLIAM B. LYBROOK, Young America, Ind., to Miss Betty Lou Etnire of Logansport, June 25.

EDMOND CHADWICK CAMPBELL, Morganza, La., to Miss Edna Peresich at Monroe, August 4.

LLOYD E. ROSENBAUM, Anderson, Ind., to Miss Doris Nussbaum of St. Louis, August 5.

MARVIN R. DAVIS, Letts, Ind., to Miss Martha Louise Banister of Columbus, July 6.

RICHARD L. VARCO, Minneapolis, to Miss Louise Miller at Pasadena, Calif., June 4.

WILLIAM B. ARMSTRONG to Miss Henrietta Collier, both of Atlanta, Ga., August 1.

STANLEY LLOYD TEITELMAN to Miss Bobette Wilson, both of Chicago, August 31.

JOSEPH RAIDER, Mundelein, Ill., to Miss Beatrice Goldsmith of Chicago, August 22.

DAVID F. STONE to Miss Katherine Charlotte Weiss, both of Indianapolis, June 28.

EMIL A. HOFER, Iroquois, S. D., to Miss Ann Hodges of De Smet, June 27.

LAWRENCE M. DUNN to Miss Gertrude Grbac, both of Depue, Ill., August 10.

Deaths

Grant Phileo Curtis ✠ Union City, N. J.; Jefferson Medical College of Philadelphia, 1906; health officer; served during the World War; for many years attending physician at the Hudson County Penitentiary; consulting phthisiologist at Margaret Hague Hospital, Jersey City; consultant at Hudson County Tuberculosis Hospital, Jersey City; aged 55; died, August 28, in the Hospital for Ruptured and Crippled, New York, of acute pancreatitis.

Lewis Leonidas Rogers Jr., ✠ Wilkes-Barre, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1913; member of the Radiological Society of North America; past president of the Luzerne County Medical Society; served during the World War; was a member of the school board of Kingston; aged 50; on the staffs of the Mercy Hospital and the Wilkes-Barre General Hospital, where he died, August 11, of arteriolar nephrosclerosis.

Guy Sexton Carpenter ✠ Waverly, N. Y.; Cornell University Medical College, New York, 1899; past president of the Tioga County Medical Society; health officer of the village of Waverly and the town of Barton; aged 66; on the staff of the Tioga County General Hospital, where he died, August 28, of cerebral hemorrhage.

George Edward Harhen, Caldwell, N. J.; Long Island College Hospital, Brooklyn, 1912; member of the Medical Society of New Jersey; at one time physician in charge of the Newark City Sanatorium, Verona; aged 53; on the staff of St. Vincent's Hospital, Montclair, where he died, August 24, of cerebral hemorrhage.

Joseph Whitman Sherer ✠ Kansas City, Mo.; State University of Iowa College of Medicine, Iowa City, 1894; University of Pennsylvania Department of Medicine, Philadelphia, 1895; fellow of the American College of Surgeons; aged 70; died, August 17, at Excelsior Springs, of injuries received in an automobile accident.

Charles Dana Hunter, Tacoma, Wash.; Rush Medical College, Chicago, 1905; member of the Washington State Medical Association and the North Pacific Surgical Association; fellow of the American College of Surgeons; served during the World War; aged 60; died, August 5, of coronary thrombosis.

Joseph Archibald Robertson ✠ Dallas, Texas; University of Texas School of Medicine, Galveston, 1898; fellow of the American College of Surgeons; attending surgeon, St. Paul's, Dallas Methodist and Baylor hospitals; consulting surgeon to the Parkland Hospital; aged 65; died, August 18, of coronary occlusion.

Oscar Ewing Townsend, Elyria, Ohio; Eclectic Medical College, Cincinnati, 1911; Medical Department of the University of Cincinnati, 1912; member of the Ohio State Medical Association; served during the World War; on the staff of the Elyria Memorial Hospital; aged 54; died, August 17, of heart disease.

James Monroe Peterson, Spruce Pine, N. C.; Tennessee Medical College, Knoxville, 1902; veteran of the Spanish-American and World wars; at one time postmaster; formerly county superintendent of public instruction; aged 68; died, August 19, in Johnson City, Tenn., of carcinoma of the lung.

Cornelius Wilson Lane ✠ Castle Rock, Wash.; Hahnemann Medical College and Hospital, Chicago, 1905; at one time health officer of Del Norte County, Calif.; for many years a member of the United States Indian Service; aged 56; died, August 13, at Longview, Wash., of coronary thrombosis.

Thomas Scholz ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1916; aged 58; on the staffs of St. Joseph's Hospital, New York Foundling Hospital and St. Francis Hospital, where he died, August 28, of diabetes mellitus and chronic nephritis.

William Baird Andrews ✠ Kent, Ohio; Homeopathic Hospital College, Cleveland, 1890; for many years member of the county board of health, president of the board of health of Kent and member of the board of education; aged 73; died, August 28, of angina pectoris.

James Tertius Norton, Kent, Ohio; Western Reserve University Medical Department, Cleveland, 1910; served during the World War; formerly on the staff of the Babies Hospital, Cleveland; aged 56; died, August 27, of coronary thrombosis and cerebral embolus.

John David Gable, Lake City, Fla.; University of Nashville (Tenn.) Medical Department, 1908; served during the World War; aged 67; on the staff of the Veterans Administration Facility, where he died, August 13, of arteriosclerosis and coronary heart disease.

Edward Lowell Saylor ✠ Akron, Ohio; University of Kansas School of Medicine, Kansas City, 1925; member of the American Society of Clinical Pathologists; aged 39; on the staff of the City Hospital, where he died, August 10, of a self-inflicted bullet wound.

Edward King Tyler, Muscatine, Iowa; State University of Iowa College of Medicine, Iowa City, 1882; member of the Iowa State Medical Society; aged 81; on the staff of the Benjamin Hershey Memorial Hospital, where he died, August 3, of chronic bronchitis.

Willard McKenzie Burleson, Richmond, Va.; Medical College of Virginia, Richmond, 1937; member of the Michigan State Medical Society; resident, Medical College of Virginia, Hospital Division; aged 28; was killed, August 31, in an airplane accident.

Nils Olof Byland ✠ Battle Creek, Mich.; University of Michigan Medical School, Ann Arbor, 1922; served during the World War; for many years on the staff of the Battle Creek Sanitarium; aged 59; died, August 29, of heart disease.

John William Leo Brennan, St. Louis; St. Louis College of Physicians and Surgeons, 1906; aged 58; died, August 28, in the Veterans Administration Facility, Jefferson Barracks, of hypertensive and coronary arteriosclerotic heart disease.

Ernest Gollub, Staten Island, N. Y.; Jefferson Medical College of Philadelphia, 1937; on the staff of the Sea View Hospital; aged 28; died, August 27, in the Post-Graduate Hospital, New York, of mastoiditis and brain abscess.

Theodore Perry Bishop, Grand Rapids, Mich.; University of Michigan Medical School, Ann Arbor, 1921; member of the Michigan State Medical Society; aged 51; died, August 29, in the Butterworth Hospital of tumor of the right adrenal.

Samuel Albert Jones, Sheffield, Vt.; University of Vermont College of Medicine, Burlington, 1883; member of the Vermont State Medical Society; aged 83; died, August 11, of cerebral hemorrhage and arteriosclerosis.

Rolla Camden, Parkersburg, W. Va.; Jefferson Medical College of Philadelphia, 1897; on the staff of the Camden-Clark Memorial Hospital and St. Joseph's Hospital; aged 67; died, August 22, of chronic nephritis.

Henry Gray Morris ✠ Jamestown, N. Y.; Cornell University Medical College, New York, 1921; member of the Radiological Society of North America, Inc.; aged 44; died, August 20, of cerebral hemorrhage.

John Ralph Coryell, Kansas City, Mo.; University of Virginia Department of Medicine, Charlottesville, 1909; aged 54; died, July 9, in St. Luke's Hospital of ruptured esophageal varices and cirrhosis of the liver.

Robert James McDonald, Doylestown, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; aged 69; died, August 17, in Columbus of pernicious anemia.

Frank James Pherson, Manchester, N. H.; Jefferson Medical College of Philadelphia, 1908; member of the New Hampshire Medical Society; aged 59; died, August 27, in Boston of heart disease.

Paul Martin Lennox, Colorado Springs, Colo.; Columbia University College of Physicians and Surgeons, New York, 1903; aged 59; died, August 28, in the Beth-El General Hospital of pneumonia.

Austin Emery St. Clair, Framingham, Mass.; University of Vermont College of Medicine, Burlington, 1893; member of the Massachusetts Medical Society; aged 75; died, August 7, of arteriosclerosis.

John Wesley Barkley, Ligonier, Pa.; Jefferson Medical College, Philadelphia, 1897; member of the Medical Society of the State of Pennsylvania; aged 72; died, August 29, of cardiovascular disease.

Thomas Blair, Ann Arbor, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; aged 79; died, August 28, in the University Hospital of perforated duodenal ulcer.

J. Thomas O'Toole, Oklahoma City; Independent Medical College, Chicago, 1898; aged 79; died, July 7, in St. Anthony Hospital of arteriosclerosis and heart disease.

Correspondence

CARBOHYDRATES AND HEADACHE

To the Editor:—With reference to the relationship between the ingestion of carbohydrates and the development of headaches, you make the statement (Queries and Minor Notes, THE JOURNAL, July 6, p. 75) that Wagner-Jauregg and Porges purported to show that a low carbohydrate diet is beneficial in cases of migraine. This suggestion was first made by me (A New Approach to Dietetic Therapy, Boston, R. G. Badger, 1933; A New Aspect of Migraine and Certain Related Conditions, *Am. J. Digest. Dis. & Nutrition* **1**:359 [Aug.] 1934, and so on), as admitted by Wagner-Jauregg in a personal communication. I offered the theory that low carbohydrate diet is effective in the prevention of migraine by preventing the development of cerebral edema. A recent publication (Migränebehandlung mit kohlehydratarmer Diät, *Klin. Wchnschr.* **18**:390 [March 18] 1939) summarizes my observations and theories and contains the pertinent bibliography.

EUGENE FOLDES, M.D., New York.

BUNDLES FOR BRITAIN

To the Editor:—The situation in England is one of intense suffering. Surgical instruments and equipment are urgently needed NOW. Will you please help me to help the doctors and surgeons at home to relieve this suffering by publishing this letter together with the enclosed list of instruments? This list has just been flown across to me by clipper, from a source of highest authority in London.

Instruments Urgently Needed in British First Aid Stations

Airways, endotracheal	Gorget, lithotomy	Speculums, ear, eye, nasal, rectal
Apparatus, anesthetic (portable)	Gouges, bone	Sphygmomanometer, aneroid
Apparatus, intravenous	Headbands, metal, with mirrors	Stands for irigators
Aspirators	Hemostats, all types	Sterilizers, all
Autoclave	Holders, needle	Stethoscopes
Basins	Inhalers, chloroform	Stools, anesthetists', with revolving top
Cabinets, instrument	Knives, all types	Stools, foot
Cannula, brain exploring	Lamps, operating, emergency, complete	Syringes, all sizes, with needles
Catheters	Mallets, metal, lead filled	Tables, instrument
Chisels, bone	Mirrors, laryngeal	Tables, operating
Clamps, bone plating	Pharyngoscope with battery in handle	Trocars
Clamps, intestinal	Plates, bone	Tubes, tracheotomy
Clips, towel	Pliers, side cutting, 6 inch	Wax, bone, sterile
Curets, mastoid	Probes, all types	Buckets
Diagnostic sets	Retractors, all types	Clippers, hair
Depressors, tongue	Rings, laparotomy	Cups, medicine
Directors, grooved, with myrtle leaf	Saws, all types	Jugs, graduated
Drill, bone	Scissors, all types	Measures, glass, graduated
Drills, cranial	Screws, bone plating	Pans, bed, enamel
Elevators	Shears	Pitchers, 3 quart
Forceps, artery, all types	Snares	Stoves, petrol or paraffin, table model
Forceps, bone, rongeurs	Sounds, metal	Tables, bedside
Gags, mouth, Denhart	Spatula	Urinals, E. I.

I feel this is the quickest way to appeal to all doctors in the hope that they will read this and send their surplus instruments to me at the address below. All contributions will be sent to England at once, where they will help to save many lives that may otherwise be lost.

RAFAELLE LEINSTER,
The Duchess of Leinster,
Surgical Supplies,
745 Fifth Avenue,
New York.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

FORMALDEHYDE STERILIZATION OF FOOTWEAR

***To the Editor:*—Please give detailed directions for fumigating shoes with formaldehyde.**

M.D., Illinois.

ANSWER.—Shoes, slippers and other footwear should be sponged each week with 10 per cent solution of formaldehyde or they can be placed in a closed box together with a dish of solution of formaldehyde for twenty-four hours. After each sponging or exposure to the formaldehyde fumes, articles should not be worn before airing for at least twenty-four hours. Failure to carry out the last precaution may result in a dermatitis from the formaldehyde vapor. Henderson and also Ayres, Anderson and Youngblood have found formaldehyde vapor an effective means of fumigation.

Cotton socks worn by patients with tinea pedis should be boiled for ten minutes or immersed for half an hour in a 1:1,000 solution of mercury bichloride. They may then be washed with soap and water or sent to the laundry. Woolen and silk stockings may be ruined by boiling, but the use of formaldehyde vapor in a box will be found effective.

References:

Henderson, Yandell: Fungous Infection of the Feet, *Arch. Dermat. & Syph.* **26**: 710 (Oct.) 1932.

Ayres, Samuel, Jr.; Anderson, N. P., and Youngblood, Esther M.: Fumigation as an Aid in the Control of Superficial Fungous Infections, *ibid.* **24**: 283 (Aug.) 1931.

SHIPPING BLOOD FOR AGGLUTINATION TESTS

***To the Editor:*—What is the opinion of hematologists on the cross-matching value of both red blood cells in a 2 per cent sodium citrate solution of physiologic solution of sodium chloride and blood serum which has remained at temperatures such as might be encountered in the ordinary methods of transportation? If such cells and serum had remained for twenty-four hours at a temperature ranging from 90 to 100 F. would these both still be suitable in cross-matching prior to transfusions?**

M.D., Oklahoma.

ANSWER.—Red blood cells in suspension in sodium citrate solution or physiologic solution of sodium chloride together with the blood serum, when shipped through the mails, are not suitable for grouping or cross-matching tests for transfusion. The best method to ship blood is to collect the blood as for a Wassermann test and send the clotted blood sample by air mail, special delivery, if the destination is any considerable distance away. The package should be marked "Avoid excessive heat and cold." The blood should be taken with sterile precautions, placed in sterile tubes and hermetically sealed with a sterile rubber stopper or in the flame. Under these conditions twenty-four hours at from 90 to 100 F. probably will not spoil the sample, there being no bacterial contamination. Blood cells in dilute suspension quickly lose their sensitivity for agglutination, even if sterile, whereas in the clotted form this is retained for much longer periods. In addition, dilute blood suspensions, especially when infected with certain bacteria, may become "panagglutinable" and are also more apt to agglutinate spontaneously or hemolyse.

As far as the serum is concerned, agglutinins will deteriorate gradually at 90 to 100 F., though the common iso-agglutinins α and β should be demonstrable for at least a week and usually much longer under such conditions, provided the sample is not infected. Not infrequently, however, the iso-agglutinins are of low titer and such will deteriorate rapidly. Moreover, irregular agglutinins, which are almost invariably of low potency, despite the fact that they can give rise to severe hemolytic reactions even though the groups of patient and donor are identical (Wiener, A. S., and Peters, H. R.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group, with Three Cases in Which the Same Agglutinogen was Responsible, *Ann. Int. Med.* **13**:2306 [June] 1940) will probably not be demonstrable under these conditions.

Accordingly the best method, as stated, is to ship the blood in clotted form. The individual receiving the sample can

separate the serum by centrifuging. Blood suspensions can be prepared by shaking up the clot in saline solution; the coarser particles are allowed to sediment and the supernatant smooth emulsion is transferred to a clean tube for use in the grouping tests.

FUNGOUS INFECTION OF NAILS

To the Editor:—I have recently seen two cases of fungous infection of the finger nails. I have not yet received reports of the cultures which have been made. Any information you may have regarding this condition, particularly as regards effective treatment, will be appreciated.

M.D., Kentucky.

ANSWER.—Infection of the nails by fungi was formerly considered a rarity, but the experience of all dermatologists contradicts this. Whether the infecting organism is one of the yeastlike fungi or belongs to the hyphomycetes the symptoms are apt to be much the same, though the yeastlike organisms are more liable to cause acute inflammation, involvement of the nail folds and pus formation. Oláh (Neuere Beiträge zur Klinik u. Therapie der Mykogenen Onychien u. Paronychien, *Dermat. Wchnschr.* **103**:1189 [Aug. 29] 1936) has emphasized the fact that stippling of the nail, Beau's punctae, as seen in psoriatics, is sometimes one of the signs of such infection. In both infections, thickening of the nail, discoloration, fissuring, scaling, brittleness, partial or complete separation from the nail bed, thinning or even almost complete destruction may be seen. Sulzberger and Lewis (Leukonychia Tricophytina, *M. Rec.* **146**:305 [Oct. 6] 1937) have reported white spots which consist of masses of spores and mycelium in the lower part of the nail next the nail bed, caused by Tricophyton gypseum.

The treatment of these cases is one of the difficult problems of dermatology. In cases in which the yeastlike infection is brought on by constant immersion of the hands in dish water or in fruit juices, as described by Kingery and Thienes (Mycotic Paronychia and Dermatitis, *Arch. Dermat. & Syph.* **11**:186 [Feb.] 1925) abstention from the work and mild applications, such as a 10 per cent solution of sodium thiosulfate in water may suffice; but most cases require more energetic measures. Puncture of the nail, if pus is seen beneath it, and wet dressings of the thiosulfate solution, painting with 5 per cent watery solution of gentian violet, or the use of mercurials such as ammoniated mercury ointment may succeed in producing cure. Iodides by mouth or sodium iodide intravenously, with tincture of iodine applied locally, is successful in some cases. In all chronic forms of either yeastlike or hyphomycetic infection the nail must first be thinned, either by direct scraping or by filing, or by first softening it by soaking it in soap solution for twenty-four hours or the application of a strong potassium hydroxide solution for a short time (45 per cent solution for fifteen minutes). The nail folds should be protected by petrolatum. This thinning process must be repeated once or twice a week. After this thinning has been carried as far as practical, three methods are open to the physician: chemical attack, actinic action or surgical ablation of the nail.

Chemical methods are many besides those already mentioned. Stelwagon applied a 0.2 to 1 per cent solution of mercury bichloride in water followed by ammoniated mercury ointment. Harrison used a 50 per cent solution of potassium hydroxide in water, to eight parts of which he added one part of potassium iodide, for softening. This he allowed to act for fifteen minutes. He then applied a 1 per cent aqueous solution of mercury bichloride for twenty-four hours. Glaze used a saturated aqueous solution of sodium thiosulfate; others apply diluted acetic acid and then mop on a 6 to 10 per cent solution of the thiosulfate. Dubreuilh advocated the application of equal parts of pyrogallol and olive oil. Sutton advocates the use of 10 per cent silver nitrate solution in alcohol. It must be a somewhat diluted alcohol to dissolve this amount of silver nitrate. Cleveland White uses a strong Whitfield ointment, 12 per cent of salicylic acid and 24 per cent of benzoic acid. Way uses 1 per cent malachite green, 2 per cent phenol, 5 per cent salicylic acid and 24 per cent alcohol in xylene, painted on twice daily. Walker dresses the nail with Fehling's solution for two days, then removes the nail and applies a dressing of 2 per cent copper sulfate in water.

Combining chemical with actinic action is the method of Paulina Gomez-Vega, who determined by a careful research that a solution of mercurochrome 1 part to 10,000 sensitizes the organisms to the action of sunlight. Her results in a small number of cases were encouraging. (Effect of Irradiation and Irradiation plus Sensitization on Yeastlike Fungi and Related Organisms, *Arch. Dermat. & Syph.* **34**:961 [Dec.] 1936).

MacKee (X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 480) uses hot soap suds for softening the nail, soaking it for an hour or two, then scraping it as thin as possible. For two weeks preceding the treatment, during the period of irradiation or for two weeks after the series of treatments has ended, he does not allow the use of any strong chemicals. While he thinks that a 1:5,000 solution of mercury bichloride, a 3 per cent ammoniated mercury ointment or 3 per cent precipitated in sulfur ointment would be permissible, he does not allow his patients to use anything stronger than soap and water.

Because of the absorption of rays by the nail plate in spite of the reduction in its thickness, some filtration of the x-rays is called for and a larger dose of rays is advisable over the nail than could be used safely on the skin. In case of combined onychia and paronychia both nail and nail fold may be first irradiated with fractional doses, then the nail fold covered by lead and an additional dose given the nail itself. He permits several nails to be treated at one exposure, both thumb nails or big toe nails, for instance. The prognosis seems better for irradiation than for chemical treatment. Relapses are not common.

Most dermatologists do not favor surgical ablation of the nail because of the frequency with which the new nail is infected.

EXTERNAL HEMORRHOIDS AND PECTINOSIS

To the Editor:—What is the treatment of varicosities of the anal margin? Can four or five varicose veins, first degree in nature, bring on symptoms severe enough to make the patient constantly uncomfortable? She complains of burning in the rectum with pains radiating to the lumbar regions and thighs. The patient, 62 years old, has a history of a number of injections for hemorrhoids. The original symptoms of protrusion and bleeding cleared up, but the pain and burning described developed and persisted for about nine months without relief. A proctologist was consulted and a diagnosis of chronic proctitis was made, due to injections made in the presence of infection. Fissure, fistula and the like were ruled out. The urine was normal. The proctoscopic examination disclosed induration throughout the wall of the rectum. This does not respond to treatment. Is it to be considered that injection of hemorrhoids may have resulted in the dilatation of the viens around the anus? Would it be safe to inject these veins with sodium morrhuate? M.D., New York.

ANSWER.—External hemorrhoids are usually unsuitable for injection treatment. In the case described it would be important to determine whether or not the varicosities are distal to the pectinate line, as injections should never be made distal to it. A pathologic thickening of fibrous tissue as a result of congestion and infection was described by W. Ernest Miles in 1918 as the pecten band and the condition was named pectenosis. It is conceivable that the injections were made into so-called mixed varicosities, obliterating the internal hemorrhoids and leaving the dilatations intact below the anal membrane or the perianal skin. The anal canal and the region of the pectinate line are extremely sensitive owing to the rich supply of sensory nerve endings. In the case mentioned chronic cryptitis or papillitis should be considered. The management of these calls for an expert proctologist.

LIPOCAIC AND LIPOLYSIN

To the Editor:—In reference to the article by Dr. Dragstedt in The Journal, January 6, can you tell me if the substance Dragstedt describes is the same as Dr. J. B. Wolffe's lipolysin? M.D., New Jersey.

ANSWER.—Lipocaic is the name suggested by Dragstedt and his associates for a substance present in extracts of pancreas which they believe represents a specific hormone concerned in the utilization and transport of body fat. The beneficial effects of the oral administration of fresh pancreas in prolonging the lives of depancreatized dogs treated with insulin and in preventing the usual fatty infiltration of the liver which occurs in these animals is due to the presence of this hormone and not to the amount of choline or lecithin present in the pancreas.

They have suggested the following criteria as indicating the presence of lipocaic in various pancreas extracts: A minimum of three normal dogs should be completely depancreatized and placed on a diet of protein, carbohydrate and liberal amounts of fat and given sufficient insulin to limit the glycosuria to less than 10 Gm. a day. The presence of lipocaic deficiency in these animals is indicated after five to six weeks by a decrease in the concentration of fat in the blood to approximately half of the

normal concentration, decrease in insulin requirement, decrease in dextrose excretion, loss of weight and appetite, impairment of liver function as evidenced by the bromsulphalein test and the finding of fatty accumulation in the liver as determined by laparotomy and biopsy. Lipocaic may be concluded to be present in a pancreas extract which when given to such animals restores the concentration of blood fat to the normal amount, restores the insulin requirement to the amount required immediately after operation, restores the average dextrose excretion, corrects the abnormality of liver function and removes the fatty accumulation in the liver, as determined by a second laparotomy and biopsy.

Wolffe has not presented this sort of evidence indicating the presence of lipocaic in his pancreas extract.

References:

Dragstedt, L. R.; Vermeulen, Cornelius; Goodpasture, W. C.; Donovan, P. B., and Geer, W. A.: Lipocaic and Fatty Infiltration of the Liver in Pancreatic Diabetes, *Arch. Int. Med.* **64**: 1017 (Nov.) 1939.

Dragstedt, L. R.: The Present Status of Lipocaic, THE JOURNAL, Jan. 6, 1940, p. 29.

UREA INJECTIONS FOR WARTS

To the Editor:—**It has come to my attention that a solution of urea has been used for injection beneath the base of ordinary warts on the hand which are incurable by any other treatment. Are there any references on the subject?**

J. Dwight Wilson, M.D., Berkeley, Calif.

ANSWER.—The only reference found to this form of treatment is "The Use of Urea (Carbamide) in the Treatment of Warts (MacKay, E. M.: *Arch. Dermat. & Syph.* **41**:736 [April] 1940). Based on the virucidal power of strong solutions of urea and their harmlessness in contact with human tissues, it was thought that the drug might be useful in the treatment of warts. Experimentation was begun by the inoculation into monkey skin of an extract of human warts in physiologic solution of sodium chloride. These injections were frequently followed by the growth of warts. An extract of warts made with a solution of urea did not cause warts in monkeys. With this as a basis, the treatment of human warts was undertaken, a 50 per cent sterile aqueous solution of urea being used. From 0.1 to 0.3 cc. of this solution was injected into the base of each wart, but not deeply. This caused pain, moderate in most instances.

The first six patients were all cured by the first injection. Of sixteen others treated by other physicians, eight were cured by one injection and several yielded to the second injection, but some of the patients resisted the treatment entirely. The cures resulted in from five to eighteen days after the injection. The author considers multiple warts more resistant than single ones. He did not treat plantar warts.

After beginning his investigation, the author discovered the report of Pietzsch in 1927, who used a method almost identical with MacKay's in the treatment of warts in horses. No reference to the use of his method in man was found.

ALCOHOL, ETHER AND ACETONE AS DISINFECTANTS

To the Editor:—**What are the relative values of the following three agents when used as skin or wound antiseptics: 70 per cent alcohol by weight, ether or acetone? In this connection it is noted that acetone is often used as a base for many of the dye antiseptic solutions. I am unable to find any definite information as to the relative value of these three agents.**

M.D., Virginia.

ANSWER.—Ethyl alcohol in 70 per cent solution by weight is an efficient skin disinfectant, especially when used with gauze friction for two or three minutes (Price, P. B.: Ethyl Alcohol as a Germicide, *Arch. Surg.* **38**:528 [March] 1939). This action is independent of any detergent quality of the solution. Disadvantages of alcohol lie in the narrow range of its strongly germicidal concentrations and the bother of preparing and maintaining solutions exactly 70 per cent by weight. Alcohol is useful in cleaning and degerming cutaneous margins of wounds, but in wounds it is painful and useless if not harmful.

Ether is a prime fat solvent, but its detergent effect on surfaces is negatived to a certain extent by rapid evaporation. An ether sponge may remove numbers of "transient" bacteria along with the grease and dirt. But ether rates low as a germicide. It is incapable of reducing the "resident" flora of the skin (Price, P. B.: Surgical Bacteriology and Technic, THE JOURNAL, Nov. 26, 1938, p. 1993). The routine use of ether as a step in preparation of the field of operation is of doubtful value. In recent freshly contaminated wounds, used with gentle friction, ether seems to have some value in preventing development of infection; it may thus improve the chances of successful primary closure of wounds. But in old chronically infected wounds it is ineffective. In this connection it is well to remember that ether precipitates proteins.

No dependable studies of the skin disinfectant action of acetone are known. But since this agent under optimal conditions in vitro is but weakly germicidal, it is not likely that the relatively small amounts present in various preparations of dyes have any disinfectant action per se. Acetone is usually added with the idea of increasing the penetrability of dyes into the skin. That it actually accomplishes this purpose is doubtful. A fact not generally appreciated is that the presence of water, even the small amounts contained in 95 per cent alcohol, causes acetone to lose its fat-solvent property.

RHEUMATIC HEART DISEASE EARLY AND LATE

To the Editor:—**A patient who was in service during the World War has a record which states that on Nov. 20, 1918, he was found temporarily unfit for overseas service on account of endocarditis. Prior to his discharge on Jan. 9, 1919, examination showed him to be physically sound with no defects. At present, physical examination shows him to be suffering from mitral stenosis with regurgitation and cardiac dilatation. The question is: Would one suffering from endocarditis be likely to recover completely within the six or eight weeks period, or is it probable that the present cardiac condition is a result of the previous attacks?**

M.D., Illinois.

ANSWER.—This case is an interesting example of the fact that one may find during active rheumatism in youth cardiac abnormalities which may retrogress or even apparently disappear entirely. There may be murmurs, particularly systolic at the apex and even middiastolic, as the result of temporary or subacute dilatation of the heart secondary to rheumatic myocarditis even before the valves are deformed. With the recovery from the acute rheumatism the heart size may return essentially to normal with the disappearance of murmurs, but continued or recurrent rheumatic infection over the years to come may result eventually in the development of real valvular deformity, especially mitral stenosis, which eventually becomes evident on examination.

This is the probability in the case referred to, but there is also the possibility that the second examination early in January 1919 might have overlooked evidence of heart involvement which was actually present at that time.

HYPOTHYROIDISM IN PREGNANCY

To the Editor:—**What should be done for a pregnant woman who displays mild symptoms of hypothyroidism and possibly hypopituitarism? She is a tertipara four months pregnant. She was sterile for five years. Anterior pituitary extract was given because of the presence of an infantile uterus and of the sterility. Significant enlargement of the uterus occurred and she became pregnant and gave birth to a normal child. Pituitary medication was given up to the first month of pregnancy. About a year and a half later, with no further endocrine therapy, she gave birth to another child, but this child at from 3 to 4 months of age displayed definite signs of hypothyroidism (cretinism). This child is still receiving thyroid.**

M.D., New York.

ANSWER.—Desiccated thyroid may be started at once and the minimum dose administered that will maintain the basal metabolism within normal limits. It would probably be safe to start with 1 grain (0.065 Gm.) of U. S. P. thyroid daily and give a little more or less, depending on the basal metabolism. It should be emphasized that the basal metabolism is elevated as much as from 25 to 30 per cent above normal in the last three months of pregnancy, making it necessary to determine the maintenance dose as well as possible in the first half of pregnancy. If animal experiments reflect the state of affairs in man, the administration of thyroid to mothers with hypothyroidism reduces the incidence of cretinism in the offspring. No pituitary extract should be given during pregnancy.

BRONCHIAL ASTHMA AND THYROIDECTOMY

To the Editor:—**A woman aged 46 complains of bronchial asthma, which started three years ago about three months after a thyroidectomy. The patient gives no history of allergy other than the asthma, which she insists was in some way or other precipitated by her operation. She even asserts that she found in some newspaper health column reference to the fact that bronchial asthma may be caused or precipitated by thyroidectomy. She has been given cutaneous tests and been found sensitive to cattle hair and horse dander and was relieved by desensitization with these allergens. Is the relation between the operation and the onset of the asthma likely to be coincidental, or is it possible that the patient's theory is correct?**

Walter Lewinnek, M.D., Mason City, Ill.

ANSWER.—There is no definite relationship between thyroidectomy and bronchial asthma. It is true that a substernal thyroid can cause wheezing by pressure on the trachea or on one of the main bronchi, in which case the wheezing would usually be found on the side of the pressure. True bronchial asthma, however, is bilateral and has no relationship to thyroid disease and thyroidectomy.

HYPERTROPHY OF GUMS FROM DILANTIN SODIUM

To the Editor:—A girl aged 20 years has had essential epilepsy since she was 15. There are petit and grand mal attacks. About twenty months ago I gave her four capsules of dilantin sodium every twenty-four hours. Previously large doses of phenobarbital did not control the attacks, but the dilantin sodium, taken with vitamin C, has been satisfactory, except for a gradually increasing hypertrophy of the gums. This condition has lately become so acute that I have had to stop the dilantin sodium. The attacks of epilepsy have almost immediately become acute again. I should appreciate any advice as to the treatment of the hypertrophy and suggestions as to the advisability of continuing the treatment with dilantin sodium. Is there anything new on the treatment of the gum condition? Is there danger of this condition not yielding to treatment if dilantin sodium is given regularly?

M.D., Georgia.

ANSWER.—Hypertrophy of the gums is a recognized complication of treatment with dilantin sodium in children. Recent investigations have shown that the process is entirely different from that seen in scurvy and that it bears no relationship to the vitamin C level. Aside from the appearance of the gums, the hypertrophy appears to do no harm, even when it persists over years. It is often preferable to the attacks.

It might be worth while to try substituting phenobarbital 0.1 to 0.2 Gm. daily for a similar amount of dilantin sodium. A vigorous outdoor life is often beneficial.

References:

Kimball, O. T., and Horan, T. N.: The Use of Dilantin in the Treatment of Epilepsy, *Ann. Int. Med.* **13**: 787 (Nov.) 1939.

Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in Treatment of Convulsive Seizures; Toxic Symptoms and Their Prevention, *Arch. Neurol. & Psychiat.* **42**: 1053 (Dec.) 1939; Further Experiences with the Use of Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, *Am. J. Psychiat.* **96**: 1023 (March) 1940.

ABSENT KNEE JERKS IN DIABETES

To the Editor:—What is the basis for absent knee jerks in the diabetic?

Samuel G. Slo-Bodkin, M.D., Brooklyn.

ANSWER.—The common cause of absent knee jerks in diabetes is neuritis (neuronitis). The explanation for its frequent occurrence in diabetes is not entirely clear except that it is in some way due to the effects of diabetes on the central nervous system. Other conditions responsible for absent reflexes may be present coincidentally.

SUBACUTE BACTERIAL ENDOCARDITIS

To the Editor:—1. Has there been any definite value in transfusion of blood from a patient who has recovered from Streptococcus viridans endocarditis? 2. Is a list of donors available? 3. By what criteria is it determined that one has recovered from subacute bacterial endocarditis? 4. Does recovery mean that the danger from embolism has passed? 5. Is the coronary artery the most likely site for embolism and is recovery possible?

W. D. Bretz, M.D., Huntingburg, Ind.

ANSWER.—1. There has been a great deal of newspaper publicity implying that blood transfusions from a patient who has recovered from Streptococcus viridans endocarditis are curative. There is no adequate evidence that such transfusions have resulted in cure.

2. So far as known, no list of donors is available.

3. Many patients experience a period of arrest, but only after two or three years of freedom from fever and absence of other symptoms can a patient be considered to have recovered.

4. There is but little danger of embolism after a three year period of freedom from all symptoms, although it may occur.

5. The coronary artery is not a common site of embolism, although signs of small emboli in the heart muscle have been reported post mortem not infrequently. Such emboli are not often fatal.

"BABYKIN" BOTTLE CONTAINER

To the Editor:—Lately several mothers have asked me about "Babykin" Scientific Container, made by Lockwood Products, Chicago. This container is supposed to keep a baby's formula just the right temperature for a 2 a. m. feeding, even though placed in the "babykin" at 10 p. m. We have always known that placing warm or hot milk into a vacuum bottle causes an abnormally large number of bacteria to grow and the formula to become sour within a few hours, usually producing a gastrointestinal disturbance if the baby takes such a feeding. Is there any difference between the "Babykin" and the regular vacuum bottle?

Leonard F. Bender, M.D., Philadelphia.

ANSWER.—There is some difference between the "Babykin" and the regular vacuum bottle in that liquids are put directly into the vacuum bottle while the "Babykin" is meant only to hold the baby's milk, which is stoppered in the regular baby's bottle. Milk put directly into the vacuum bottle may be contaminated by bacteria on the cork and within the bottle itself. It is not possible to sterilize the vacuum bottle, since heating will break it. Thus, milk put into a vacuum bottle and kept warm will probably sour within a short time. However, the milk in the baby's bottle which has been boiled and sterilized will not sour within a period of twelve hours or longer. The use of the "Babykin" for a reasonable period appears to be safe.

INJECTION OF TRYPSIN IN MAN

To the Editor:—Can a dilute sterile solution of trypsin (the enzyme) be injected subcutaneously into a human being without ill effects? The enzyme in the solution is active.

Maurice Vaisberg, M.D., New York.

ANSWER.—Trypsin is extremely toxic and gives rise to symptoms resembling those of snake venoms (Rocha e Silva, M.: *Arch. f. exper. Path. u. Pharmakol.* **194**: 335, 1940).

VACCINES FOR TYPHUS

To the Editor:—Is there a serum or vaccine, not experimental, for typhus fever that is now known to be effective? Our board of health is using one and I have not used it as my reports say it is not yet of proved worth.

H. A. Geitz, M.D., Monterrey, Mexico.

ANSWER.—Several vaccines prepared from tissue cultures of the specific rickettsia of typhus fever are being tried experimentally. An extensive experiment is being carried out in Europe at the present time but as yet no serum or vaccine against typhus possesses proved value.

X-RAY THERAPY FOR CARCINOMA OF PANCREAS

To the Editor:—Is x-ray treatment of any value for carcinoma of the pancreas? In the case I have in mind an anastomosis between the gallbladder and the jejunum has been done to relieve the biliary obstruction.

M.D., New York.

ANSWER.—There is no authentic evidence available to indicate that x-ray therapy is of any value for carcinoma of the pancreas.

AMBULATORY AUTOMATISM OR FUGUE

To the Editor:—The inquiry from a physician in New York in The Journal, August 10, concerning his compulsive movements and the answer suggesting a psychic epileptic equivalent interests me because it has three unusual features: 1. It occurs only at night. 2. It does not occur at night except when he goes to his office. 3. His fugue consists largely of this motor component without any accompanying dreamy state or amnesia. The length of the attack and its sudden stoppage when the physician leaves for home makes one believe there is a neurotic component. The answer considers this possibility. I wonder, therefore, why the suggestion was made for 1 Gm. of sodium bromide to be taken three times daily. May I also comment on the references. The first should be Oppenheim and not Oppenheimer. This reference is to Bruce's English translation of a rather old book which I first translated forty years ago for J. B. Lippincott & Co. The best review of the subject today is that by S. A. Kinnier Wilson, "Modern Problems in Neurology" (1928), published by Williams and Wilkins, Baltimore. Gower's book on "Epileptic Equivalents," although printed many years ago, is still the best monograph that has been written on this subject.

Edward E. Mayer, M.D., Pittsburgh.

POLIOMYELITIS AND TONSILLECTOMY

To the Editor:—In Queries and Minor Notes (The Journal, September 7, p. 877) the first reply to the question on poliomyelitis and tonsillectomy refers to a group of cases of the bulbar type reported by Aycock and Luther (*New England J. Med.* **200**: 164 [Jan. 24] 1929) as having followed tonsillectomy "by seventeen to eighteen days, an interval corresponding with the incubation period of the disease." The interval between tonsillectomy and onset of the disease in this group of cases was actually seven to eighteen days.

A second reply to the question expresses doubt as to whether tonsillectomy is a predisposing factor to infantile paralysis because of the great number of such operations performed in the fall of the year "without any apparent material increase in the number of cases of infantile paralysis." While we have seen three bulbar cases following tonsillectomy in the practice of one physician within a month (175 tonsillectomies), it is true that few or no such cases may be encountered in even a large series of tonsillectomies; but any sizable study of poliomyelitis will show a greater proportion of cases of the bulbar type following tonsillectomy by a specific interval than would occur by coincidence. For example, Eley and Flake (*J. Pediat.* **13**: 63 [July] 1938) reported that eight (2.07 per cent) of 287 patients with spinal poliomyelitis admitted to the Children's Hospital, Boston, had had tonsillectomy within a month, whereas seventeen (12.98 per cent) of 131 with the bulbar type admitted during the same period had had tonsillectomy within a month. Of greater significance was the time interval between tonsillectomy and onset of the disease in the two groups. The eight spinal cases followed tonsillectomy by seven to thirty days (random), whereas all seventeen of the bulbar cases occurred between the tenth and twentieth days following tonsillectomy. It should be noted that one patient had only adenoidectomy.

While it cannot be said that season per se constitutes a contraindication to tonsillectomy, it is clear that the avoidance of this operation where poliomyelitis is prevalent undoubtedly would prevent the occurrence of a number of cases of this distressing and highly fatal form of the disease each year.

W. Lloyd Aycock, M.D., Boston.

Harvard Infantile Paralysis Commission.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, September 28, page 1123.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, February. Part III. Baltimore and New York during October and Boston during November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various centers, Feb. 20. Final date for filing application is December 21. *Oral.* Cleveland, May 31-June 1. Final date for filing application is April 1. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral.* Chicago, Dec. 6-7. Applications for Group A must be on file not later than Nov. 1. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Parts 1-A and 1-B, Feb. 17. Final date for filing application is Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Part I Group B examinations, locally, Jan. 4, 1941, at 2:00 P. M. Final date for filing application is Oct. 5. Part II, Groups A and B, Cleveland, Ohio, June 1941, immediately prior to opening of A. M. A. meeting. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Cleveland, Oct. 5. *Written.* Various centers, March 8. *The only written examination during 1941.* Applications must be on file not later than Dec. 1. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written.* New Orleans, January 1941. Final date for filing application is November 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31, following the Region I meeting of the American Academy of Pediatrics. Chicago, May 18, following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, December 18-19. Final date for filing application is October 10. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF UROLOGY: *Oral and Written.* Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Missouri June Report

Dr. Harry F. Parker, secretary, State Board of Health of Missouri, reports the written examination held for medical licensure at St. Louis, June 6-8, 1940. The examination covered fifteen subjects. An average of 75 per cent was required to pass. One hundred and sixty-one candidates were examined, all of whom passed. Twelve physicians were licensed to practice medicine by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1940)	88.8
Northwestern University Medical School	87.7, 87.8, 88.2, 88.4	(1930) 88.4, (1940)	81,
Rush Medical College		(1939) 88.6,	90
University of Illinois College of Medicine		(1940) 86,	89.2
University of Kansas School of Medicine		(1937)	85
Univ. of Louisville School of Medicine		(1938) 88.2, (1939)	88.7
Tulane University of Louisiana School of Medicine		(1939)	87.3
Harvard Medical School		(1937)	89.5
St. Louis University School of Medicine	(1940) 81.7, 82.2, 83.5, 83.6, 83.8, 84, 84.2, 84.2, 84.7, 84.7, 84.8, 84.8, 85, 85.2, 85.3, 85.3, 85.4, 85.5, 85.6, 85.6, 85.6, 85.6, 85.8, 85.8, 85.9, 86.4, 86.4, 86.4, 86.4, 86.6, 86.6, 86.7, 86.7, 87, 87.1, 87.2, 87.2, 87.4, 87.4, 87.5, 87.6, 87.9, 88, 88, 88.1, 88.3, 88.4, 88.4, 88.6, 88.7, 88.7, 88.8, 88.8, 88.9, 88.9, 89.1, 89.2, 89.2, 89.5, 90.1, 90.7	(1938) 90.7, (1939)	85.2,
Washington University School of Medicine	82.4, 83, 83.9, 84, 84.2, 84.2, 84.4, 84.4, 84.5, 84.5, 85.2, 85.2, 85.6, 85.7, 85.8, 85.9, 86, 86, 86.1, 86.1, 86.2, 86.2, 86.3, 86.4, 86.5, 86.5, 86.6, 86.6, 86.o, 86.6, 86.6, 86.7, 86.7, 86.8, 86.8, 86.8, 86.9, 87, 87, 87, 87.1, 87.2, 87.2, 87.3, 87.3, 87.3, 87.4, 87.5, 87.5, 87.6, 87.6, 87.6, 87.8, 87.8, 88, 88.2, 88.2, 88.3, 88.4, 88.6, 88.6, 88.8, 89, 89.2, 89.4, 89.4, 89.5, 89.6, 89.7, 89.7, 89.9, 89.9, 90.6, 91.2	(1937) 88, (1940)	82.3,
Creighton University School of Medicine		(1940)	85.9
University of Nebraska College of Medicine		(1939)	86.8
University of Oregon Medical School		(1939)	88
Jefferson Medical College of Philadelphia		(1938)	86.7
University of Toronto Faculty of Medicine		(1939)	89.8

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1939)	Arkansas
Loyola University School of Medicine		(1939)	Kansas
Univ. of Kansas School of Medicine		(1926), (1931), (1939)	Kansas
University of Louisville School of Medicine		(1933), (1939, 2)	Kentucky
University of Nebraska College of Medicine		(1939)	Nebraska
Ohio State University College of Medicine		(1939)	Ohio
University of Cincinnati College of Medicine		(1932)	Ohio
Meharry Medical College		(1924)	W. Virginia

Book Notices

The Australian Army Medical Services in the War of 1914-1918. Volume II: The Western Front. By Colonel A. G. Butler, D.S.O., V.D., B.A. Cloth. Price, 21s. Pp. 1,010, with 212 illustrations. Canberra: Australian War Memorial, 1940.

This volume is concerned chiefly with the operations of the Australian army medical service on the western front, 1914-1918. The book is divided into three sections and fourteen appendixes.

Section I is a narrative of those aspects and events in which the Australian forces directly participated until the end of 1917. The course of the fighting is followed chronologically from the preliminary sorties and feints leading up to the battle of the Somme until the third battle of Ypres. The battle of Cambrai, big in its import and omen if slight in its direct effects, completed the old and points the new phase of the war.

Section II examines, from an objective service standpoint, the fundamental problems of the prevention of disease and of the rescue, repair and return to duty of casualties. Accordingly, the chapters of this section follow the course of a casualty from the regimental aid post through the various stages and levels of transport and treatment in the field, at the expeditionary base and at home, to the command depots and overseas training brigade. A final chapter of the section examines the technic of disease prevention.

Section III resumes the narrative of the experiences of the Australian army medical service on the western front. The successive blows in the British advance up the Somme to the Hindenburg line are described. The dual task facing the Australian medical service is clearly brought out. Within eight weeks it was necessary to deal with one seventh of the total battle casualties and to sustain the chief part in the problem of maintaining the fighting formations at a strength adequate for these stupendous tasks—and this in the face not only of casualties but of pandemic influenza. Not the least significant feature of the Australian army medical service in the war is revealed in the fact that, of the effectives that reached the front, no less than 60 per cent were recovered men.

As related in this volume, the salient lessons that seem to emerge from the Australian experience in the evacuation of wounded in the great war may be thus summed up: 1. In any great battle a proportion—which may be estimated at some 2 to 5 per cent—of all casualties other than from gassing will, if their lives are to be saved, require special arrangements for insuring early operation or for effective first aid at a field or mobile hospital. 2. For the rest, success in evacuation is in a great measure determined by the exact and early discrimination of stretcher cases, "sitters" and "walking wounded" and the making of special and adequate arrangements for the transport and treatment of each class. 3. The basic principle, to insure successful evacuation under all conditions and every combination of circumstance, the medical scheme must adapt its arrangements to the fundamental constants, physical, physiologic and pathologic, which lie, and will always lie, behind the particular problems of all types of warfare and of every battle.

This volume has mirrored truly the interplay of the constant factors that compose the medical problem—time and distance, mass and movement, human powers and human limitations—which are common to any type of warfare. Only one feature prevents this volume from being an intensely interesting and readable work. Too many abbreviations cause too many interruptions to those unfamiliar with the British medical evacuation system; otherwise this volume may be recommended to any one studying or contemplating active medical field service as a mine of exact information.

Localisations viscérales et aspects chirurgicaux des brucelloses. Par R. Michel-Béchet, associé national de l'Académie de chirurgie. Avec la collaboration de MM. R. Puig et P. Charvet. Préface du Pr R. Cunéo. Paper. Price, $1.15. Pp. 168, with 22 illustrations. Paris: Masson & Cie, 1939

It is gratifying to American investigators of human brucellosis in its varied forms to find in so valuable a book as that of Michel-Béchet and his collaborators that these French authors have discarded the former designations of the disease—Malta, or undulant, fever—names which were probably to some extent responsible for the failure to recognize phases of the disease which occur without significant rises in temperature. The authors emphasize that there is no definite pattern of brucellosis. Nothing is more fantastic, they say, than the evolution of this disease. The onset may be insidious, or an attack of indigestion suggests intestinal grip; or pain in the joints suggests rheumatism, and it is only after the attacks have been repeated a few times that one thinks of brucellosis.

Four cardinal signs are mentioned as characteristic of the septicemic phase of brucellosis: temperature, pain, perspiration and weakness. The rises in temperature may occur in waves (which suggested the name "undulant fever"). But the undulating temperature curve is not a constant feature. It may vary in intensity; the undulations may proceed without intervals; after weeks or months of apparent health a new wave may appear. The French have a name for it: "lunatic fever." There is an uncertainty as to whether brucellosis can occur without fever, because in some cases observations of temperature are not made in the initial period, which may be more or less ignored. The afebrile form of the disease is encountered especially in children. The painful manifestations of brucellosis are extremely varied. They may involve joints, nerves or subcutaneous tissues. Asthenia is an important feature. It may deprive the patient of all energy or desire for a normal life, persisting for a long time without accompanying fever, pain or perspiration. A psychic factor may be involved in the asthenia. The patient who has been disabled for a long time, discouraged by persistent pain and disappointed with the failures of therapy may fall into a kind of apathetic resignation. Sometimes after long periods of asthenia there will be a relapse, with localization of the infection.

Orchitis occurs in about 20 per cent of cases. The genital organs of the female are less frequently affected. Although in domestic animals abortion is a unique manifestation of brucellosis, in women brucellar infection seems to have no more effect on gestation than any other septicemia. Anemia with leukopenia and monocytosis with polymorphonuclear leukocytes falling to 40 or 50 or even as low as 20 per cent form a characteristic blood picture. Epistaxis is a frequent symptom. Other symptoms observed are indigestion with stubborn constipation, anorexia, diarrhea in severe cases, enlarged liver and, less frequently, enlarged spleen. The heart and kidneys are rarely affected. These symptoms characterize the average case. The authors emphasize, however, that the disease cannot be codified. The book describes other manifestations which occur irregularly and are of little diagnostic value.

Convalescence is prolonged. After apparent recovery a new wave of fever may occur with or without a return of the original symptoms or with painful osseous or nervous complications. Brucellosis presents an infinite variety of evolutions which may be violent or mild. In certain parts of France the disease is a veritable social scourge. Whether there is ever complete recovery from brucellosis is a question the authors raise without answering, except by citing cases in which there were recurrences long after apparent recovery.

The authors found it difficult to estimate the percentage of cases of brucellosis in which complications develop because, as a rule, patients with uncomplicated brucellosis do not enter the hospital. They state, however, that in 80 per cent of cases with localization of the infection the localization was preceded by a recognizable septicemic phase of the disease.

Brucellar hepatitis is the most frequent localization. It can be the only manifestation of the infection. At the time of the third or fourth wave of fever the liver may increase in volume and become painful; diverse hemorrhages may appear—bleeding gums or purpura especially on the lower limbs, associated or not with edema. These symptoms and the various complications which may be associated with them are discussed in detail, with case reports. Brucellar infection can invade the biliary tract, causing angiocholitis or cholecystitis. The authors believe they are the first to report that brucellar infection may be the cause of biliary lithiasis.

Nervous complications are second in order of frequency. They resemble the nervous symptoms of syphilis more closely than those of any other infectious disease. The different aspects of neurobrucellosis, with detailed discussion and case reports, are enumerated: (1) the encephalitic syndrome, (2) the medullary syndrome, (3) the peripheral syndrome, (4) the meningeal syndrome. Any one of them may be acute or chronic. A chapter is devoted to respiratory complications. Brucellar laryngitis, tracheobronchitis, pulmonary congestion all resemble tuberculous infections. Errors in diagnosis are frequent. In a section of the book entitled "Surgical Aspects of Brucellosis" are included visceral, osseous and osteo-articular localizations, with separate chapters devoted to the complications which are of especial interest—facial lesions, osteoperiostitis, osteo-arthritis, coxitis, spondylitis.

The dry black facial lesions have a marked predilection for the area over the body of the jaw in front of the masseter. They may be bilateral. The topography and behavior of these lesions are so precise that a retrospective diagnosis of brucellosis may sometimes be made in cases in which the correct diagnosis was missed. Cases in which the facial lesions develop are usually severe and end fatally.

Osteoperiostitis may develop in the course of the second or third wave of fever or early in convalescence. In some cases it is the only manifestation of the disease.

Osteo-arthritis seems to occur most frequently in young people. Localization in the hip is most frequent, followed by the knee, the elbow, the shoulder and the sacro-iliac joints. The inflammatory lesions may be acute or chronic. They usually develop during convalescence and accompany a recurring septicemic episode. But they can be the only manifestation of a relapse with no rise in temperature or they may mark the beginning of the disease. In such cases errors of diagnosis can easily be made. Clinically the osteo-arthritis of brucellosis may be subacute or chronic, resembling tuberculosis; or acute, resembling a gonococcic infection. The pain may be violent. As a rule, however, there is an absence of suppuration and ankylosis.

Reports of three cases of coxitis are given. In one of them there had been no fever for three years previous to the development of the painful joint; in one there was no other manifestation of brucellosis; the third case was extremely acute, with the temperature rising to 40 C. (104 F.).

Under the term spondylitis the authors designate all localizations in the vertebral column detectable by x-ray examination, whether osseous or osteo-articular, acute or subacute, excluding the simple vertebral reactions of brucellar septicemia, which are almost constant. The subject is treated extensively, with many reproductions of roentgenograms. Spondylitis occurs much more frequently in men than in women; it occurs especially in patients past 40. The lumbar region is most frequently affected. Sometimes spondylitis develops long after the septicemic episode; it may be unaccompanied by an elevation of temperature. The patient may be incapacitated six or eight months or more.

Brucellosis is fatal in only 2 to 4 per cent of cases. Its seriousness lies in the length of evolution, in the painful manifestations and in the persistent weakness it leaves. It ruins poor people.

The responsibility which should be assumed for veterinarians, dairymen and others who are infected in line of duty is discussed, together with the difficulties involved. In the case of slaughterhouse workmen in cities, where the foyer of infection is known, the difficulties of authentication are relatively slight. On the contrary, in rural districts where there is the possibility of contracting infection from food or various objects soiled by infected animals, it would be almost impossible to prove that the infection was contracted in line of duty.

The authors discuss the various methods of treating brucellosis under (1) anti-infectious therapy, chemical or biologic, and (2) symptomatic therapy. They do not heartily endorse any of the

proposed methods of anti-infectious therapy. On account of the irregular evolution of the disease they are always skeptical, they say, in reading statistics of therapeutic successes. Nourishment should be substantial. The authors insist that even patients with high temperature must take as much nourishment as possible. Each physician must judge for himself the best medication for the particular manifestations which he finds: for example, vitamin B for nervous complications, soporifics for patients troubled with insomnia.

Experimental Poliomyelitis. I: A Critical Review of the Literature with Special Reference to the Use of the Neutralization Test in Immunological Studies. II: The Neutralization Test. A Study of Some Factors Involved in the Neutralizing Action of Immune Serum Against Poliomyelitis Virus. By Morris Schaeffer, Ph.D., and Ralph S. Muckenfuss, M.D. Department of Health. Bureau of Laboratories, New York, N. Y. Published under the auspices of The National Foundation for Infantile Paralysis. Paper. Pp. 158. Lancaster, Pa.: Science Press Printing Company, 1940.

The authors describe their extended experience with neutralization tests in experimental poliomyelitis, which in large part consisted in 440 tests with one pool of virus and one pool of human convalescent serums. On the average, the outcome of one test out of six was irregular according to Aycock's analysis of the data, while one test out of four was irregular as judged by the criteria of Schaeffer and Muckenfuss. Thus they regard the present neutralization test as not practical for quantitative purposes and they consider that all attempts to define a minimal infective dose of virus have been unsuccessful. They reason that general epidemiologic principles but not specific immunologic problems have been elucidated by the test. They accept the widespread distribution of humoral neutralizing substances in man and a general immunologic relationship between all strains of poliomyelitic virus. They regard as unsettled the existence of specific immunologic differences among strains and they believe that a relation between protection against infection and the presence of neutralizing bodies in the blood does not hold for individuals either in the experimental or in the natural disease. In this last view they are supported by other authorities, but it is not clear that this aspect of the problem has been studied adequately with the proper epidemic strain. The original experiments presented in part II were planned to bring to light factors which might eliminate irregular results. One supply of virus was used throughout. This consisted of a glycerinated pool of spinal cords from fifty monkeys. As the experiments progressed two leads were uncovered. One concerned the use of a short needle (one fourth inch) for intracerebral inoculation and the other was the substitution of the cisterna magna for the cerebral hemisphere to receive the inoculation. It might be noted in passing that the aging of the pool of virus might have been a factor of importance also. Emphasis in the text is specialized and the book will be of most value to those interested in the technical features of the neutralization test. The bibliography contains 289 titles.

Differential Diagnosis in Internal Medicine. By Prof. Dr. Med. O. Naegeli. Authorized English translation by Simon B. Spilberg, M.D., Head of the Department of Internal Medicine, Mount Sinai Hospital, Milwaukee, Wisconsin. Cloth. Price, $10. Pp. 726, with 162 illustrations. Chicago: S. B. Debour, Publishers, 1940.

This is a good book, particularly for those specialists of internal medicine who have had sufficient background and training to appreciate symptom complexes rather than general descriptions of diseases. The author presumes that the reader is well acquainted with disease pictures and particularly with hematology and emphasizes in his preface that the importance of hematology in differential diagnosis has not been sufficiently appreciated. Throughout the entire book it is therefore noticeable that the author directs attention to the possible significance of the blood as a differential diagnostic aid. The chapters on the anemias, hemorrhagic diathesis, leukemia and allied diseases are exceedingly well presented. What is especially important is the presentation of clinical observations which have been gained only through years of experience. Such facts are most valuable to the physician in differentiating the questionable cases. An excellent illustration of this is the chapter on special differential diagnosis of pernicious anemia. It is regrettable that in these chapters there are not more illustrations of blood smears. Otherwise, however, the entire book is well illustrated with appropriate diagrams, photographs and brief but carefully selected case histories. The chapter on the symptom complex of a large spleen with gastrointestinal hemorrhage, which deals especially with chronic thrombosis of the portal vein and of the splenic vein, is commendable since the clinical picture is in general too little known but is highly characteristic. The subjects presented cover the entire field of internal medicine and diseases of the nervous system. Special comment should be made of such chapters as those on the differential diagnostic significance of electrocardiographic observations, the differential diagnosis of pains in the back and flank caused by root sciatica, lumbago, disorders of the spine, prostatic diseases and polyneuritis, the differential diagnosis of psychoneurosis from organic disease especially in insurance compensation, psychoneuroses, demand neuroses, vasomotor neuroses, encephalosis post-traumatica after skull injury and gross organic traumatic diseases of the brain. Probably the weakest chapters are those dealing with hypertension and nephritis. The book is exceedingly well printed but the binding could be improved. The translator has performed a creditable task in presenting this book to the medical profession.

The Badianus Manuscript (Codex Barberini, Latin 241) Vatican Library: An Aztec Herbal of 1552. Introduction, translation and annotations by Emily Walcott Emmart. With a foreword by Henry E. Sigerist. Cloth. Price, $7.50. Pp. 341, with 118 plates. Baltimore: Johns Hopkins Press; London: Oxford University Press, 1940.

One of the most interesting books that have appeared dealing with the early history of medicine on the Western Continent is the reproduction of the Badianus Manuscript. The original of this volume, which appeared in 1552, is in the Vatican Library. It is an Aztec herbal and is not only the earliest complete Mexican medical treatise which is known but is also the only medical text known to be the work of the Aztec Indians. The authors of the herbal were two Indians, Martinus de la Cruz, the writer of the text, and Juannes Badianus, "reader in Latin," who translated it into that language. Both men were at the College of Santa Cruz at Tlaltilulco. The original volume, of which this is a facsimile, is a small book bound in sixteenth century crimson velvet which shows the imprint of metal clasps. The Latin text of the original has been translated for this facsimile by Dr. Emily Walcott Emmart, who has included in the book an extensive and interesting introduction describing the original volume and its history as far as it is known. This introduction also discusses the colors used in the original illustrations, the nature of the pigments employed and their symbolism, together with a chapter on mythology and materia medica as they are represented in the volume. Finally there is also a description of Aztec herb gardens.

In this volume are reproduced in color the 118 pages of the herbal showing 184 illustrations of native plants and trees which were employed by the Aztecs in the practice of the healing art. These illustrations are of great interest, as they are the earliest known pictures of American botany. They are reproduced from photographs taken in the Vatican Library, the beautiful water color reproductions being the work of Madame Marie Thérèse Missonnier-Vuillemin, niece of Eugene, Cardinal Tisserant, prefect of the Vatican Library. The colors in the original paintings have been admirably reproduced by the printer Mr. A. B. Hoen. Many of the plants are difficult of recognition, as they are all drawn of one size and are lacking in perspective. As the translator, Badianus, did not know the Latin botanic names for the plants they are all labeled with their Indian names, so that the plants are in many cases hard to identify. Under each picture is the name of the disease or condition for which the plant is to be used and this is followed by a brief description of the way it is to be employed.

The work is divided into different chapters, each one treating of a certain class of disorders. For example, chapter I treats of "the head, boils, dandruff, scabies, falling hair, lacerations or fractures of the head"; chapter II of the eyes; chapter III of the ears; chapter IV of "coryza, medicine to be instilled into the nose, blood herb," and so on. Besides these and many other medical conditions for the treatment of which remedies are provided, directions are given for other states which perhaps may be considered as nonmedical. Among these is the "herb for lassitude" and "trees and flowers for the fatigue of

those administering the government and holding public office"; for the latter use some fifty drugs are mentioned, including the brains and bile of several animals, among them the coyote and the skunk. Some of the references to diseases are quite good, as for instance the discussion of the treatment of fevers, in which the main symptoms of the condition are well listed.

Naturally the remedies mentioned are by no means confined to the vegetable kingdom, as a large number of animal and mineral products are also advised. Among these as illustrations may be mentioned a purple or white stone from the stomach of a swallow, inhalation of the odor of burning hair, pebbles collected from brooks, an Indian kite and dove ground in water, and a burned heart of a stag ground in water.

Enough has been said to indicate the general character of this interesting work. It should be pointed out that the publication of the facsimile has been made possible only through the cooperation and support of the Smithsonian Institution, various garden clubs, which were interested in it on account of its being the earliest herbal of the New World, and finally a number of individuals who contributed generously to the project.

The facsimile volume is a fine example of book making and reflects great credit on the Johns Hopkins Press and the printers, A. Hoen & Co., Inc.

Principles of Hematology with 104 Illustrative Cases. By Russell L. Haden, M.A., M.D., Chief of the Medical Division of the Cleveland Clinic, Cleveland. Second edition. Cloth. Price, $4.50. Pp. 362, with 167 illustrations. Philadelphia: Lea & Febiger, 1940.

The appearance of the second edition of this excellent book one year after the first attests its popularity. There are fourteen additional pages, and more than twelve illustrations have been added. The material is presented in terms of the physiology of blood and its pathologic variation. Morphology, although emphasized, is used to describe processes and mechanisms rather than names of structures. Haden feels that "the average physician should not attempt to interpret conditions which puzzle even an experienced student of the blood" and so has omitted the technic of supravital staining and biopsy and puncture of the bone marrow. The details of technical methods of blood examination are well presented, and new and helpful features have been added. The clinical features of the diseases are brought out as the "mechanism" of the disease, and the classic features are elaborated in the case reports. Therapy is treated in the same way. The 104 cases described, if carefully studied, would constitute an excellent form of postgraduate review for the student of hematology. The photographs are unusually good, many features being brought out in black and white with the same degree of clearness as some colored pictures. The diagrams in chapters 8 and 9 illustrating the formation, circulation and destruction of red and white blood cells in various conditions are nonmedical in character and probably would be of more value to the lay student than to the average physician. It is quite possible that some hematologists will take issue with the terminology and classifications, but hematology has not yet reached the stage when differences of point of view or nomenclature necessarily mean that one author is correct and another one wrong. The book is the best introduction to hematology that is available to medical students or practitioners and, because of its excellence and simplicity, will serve to standardize many variable features which now confuse both patient and physician.

Thirty-Seventh Annual Report 1938-1940 of the Imperial Cancer Research Fund. Founded under the direction of the Royal College of Physicians of London and the Royal College of Surgeons of England, 1902. Incorporated by Royal Charter, 1939. Paper. Pp. 43. London: Royal College of Surgeons, 1940.

Gye, director of the Imperial Cancer Research Fund, reports that a large part of the cancer research concerns the induction of malignant new growths by application of pure chemical substances and points out that this aspect of carcinogenesis has occupied the attention of the scientific staff of the fund for several years. Pullinger has found that polycyclic hydrocarbons which have the property of inducing cancer evoke, on the second to the fourth day after application, a reaction which is characteristic and may be specific. The chemically related hydrocarbons which do not induce cancer formation do not evoke the reaction. Crabtree's experiments indicate that substances with the biochemical property of inhibiting cell glycolysis can, under different experimental conditions, either retard or accelerate the rate of induction of tumors by carcinogenic hydrocarbons.

The original observations of Cramer and Horning that brown degeneration of the adrenals occurs in mice which have been subjected to prolonged treatment with estrogen have been confirmed by Burrows, Lacassagne and Dobrovolskaia-Zawadskaia. Subsequent research on more extensive material, on many inbred strains of mice of high, medium, low or no cancer incidence, both by Cramer and Horning and by Dobrovolskaia-Zawadskaia, has shown that brown degeneration is not an invariable lesion present in cases of mammary cancer and that it is merely incidental to the physiologic changes which are brought about by excessive estrogenization.

Ludford has been interested in the leukocytes and macrophages which infiltrate tumors in vivo in relation to malignant growth. Leukocytes and macrophages may stimulate the proteolytic activity of the malignant cells and this might be expected to facilitate invasion of normal tissues. It is conceivable that a very intense stimulation of the proteolytic activity of malignant cells might result in a breakdown of the connective tissue framework of a tumor and bring about such a disorganization of its growth as to cause regression. Ludford has carried out experiments to explore this possibility.

Foulds is preparing a report on spontaneous fowl tumors. Two spontaneous sarcomas have been transmitted by filtrates of the original tumors. This is apparently the first recorded example of transmission of a spontaneous sarcoma by filtrate. Experiments with the nonfiltrable dibenzanthracene fowl sarcoma RFD2 by Foulds and Dmochowski indicate that there are at least two antigenic substances common to the nonfiltrable RFD2 and the filtrable Rous sarcoma and that the anti-RFD2 serums contain an antibody which reacts with the Rous tumor virus which has been repeatedly washed to remove extraneous fowl protein. The report contains a discussion of the experiments with the Shope rabbit fibroma. Knox, studying the desiccation of tissues, has achieved great improvement in the activity and the reliability of dried material by attention to the technic and principles of desiccation. He has also carried out experiments designed to analyze the nature of the filtrable agent of fowl sarcomas by feeding it as far as possible from fowl protein.

The Blood Picture in Hemorrhagic Anemia. By Jane M. Leichsenring and Alice Biester with the collaboration of Hortense Hönig Deinard et al., Division of Home Economics, University of Minnesota, Agricultural Experiment Station, Technical Bulletin 139. Paper. Pp. 120. St. Paul, Minn., 1939.

This presents, according to the authors, "a comprehensive study of blood changes occurring in hemorrhagic anemia induced in dogs maintained on a synthetic diet." The bulletin contains a large amount of data carefully obtained and presented in great detail. Physical measurements include blood volume measurements expressed in terms of cubic centimeters per kilogram of body weight; erythrocyte and leukocyte counts; determination of the hemoglobin, and measurement of the cell diameters and mean corpuscular volume. Chemical measurements include the oxygen capacity; total amino acid, nonprotein and urea nitrogen; preformed creatinine; calcium and phosphorus, and plasma protein, with albumin and globulin partition. The data and discussions are presented with regard to the three portions of the blood, the cells, the plasma and finally the whole blood and are based on the results of short and long time experiments. As a result of these experiments it is pointed out that "judgment of an individual's condition, based on hemoglobin level, red cell count or red cell hematocrit in the very early stages of recovery (after hemorrhage) would give an erroneous conception and create a false sense of security." The application of their results to the results of both acute and chronic hemorrhage in man is discussed in some detail and the similarity between the blood picture in dogs made anemic by hemorrhage and that observed in idiopathic hypochromic anemia of man leads to the suggestion that the "latter type is frequently the result of hemorrhage." The material presented together with a large bibliography makes the bulletin invaluable for those who may undertake experimental work on the blood of dogs, although no substantial contributions applicable to the anemias of man have been made.

Traité d'ophtalmologie. Publié sous les auspices de la Société française d'ophtalmologie. Par MM. P. Bailliart, Ch. Coutela, E. Redslob, E. Velter. René Onfray: Secrétaire général. Tome VIII: Thérapeutique médicale, Hygiène, médecine légale, ophthalmologie des pays chauds, ophtalmologie comparée, déontologie. Par M.M. R. Bonnardel et al. Cloth. Price, $10.50. Pp. 1,003, with 164 illustrations. Paris: Masson & Cie, 1939.

In view of what the French have had to undergo for the past year, they deserve enormous credit for the appearance on time of the eight volume treatise on ophthalmology. The preceding seven volumes have been reviewed in these columns and this last volume conforms to the others in physical characteristics. The material here is diverse and in many instances treated in a short chapter of only two or three pages, so that a general compilation will have to suffice, as follows: medical therapeutics of the eye, ocular hygiene, legal medicine, ophthalmology in the torrid countries, comparative ophthalmology and ophthalmic deontology, which latter term Webster defines as "the ethics of duty." The authors responsible for these chapters are Bonnardel of Paris, Brion of Lyons, Caillaud of Orléans, Cantonnet of Paris, Chappé of Paris, Cosse of Tours, Coutela of Paris, Gunsett of Strasbourg, Haas of Paris, Liegard of Paris, Margerin of Paris, Monthus of Paris, Pesma of Bordeaux, Plicque of Paris, Reiss of Strasbourg, Robin of Alfort and Toulant of Algiers. The entire volume is concluded with a comprehensive index of all eight volumes. The entire work is worth while. It is only natural that American ophthalmologists will disagree in many minor points and will be unable to subscribe to some of the surgical and therapeutic measures advocated On the whole, the work is thorough, well written and well illustrated and contains an adequate international bibliography. This is without doubt the last large bit of work that will appear from France for many a year and fortunately it is one of which the French may well be proud.

The Compleat Pediatrician: Practical, Diagnostic, Therapeutic and Preventive Pediatrics for the Use of Medical Students, Internes, General Practitioners, and Pediatrists. By Wilburt C. Davison, M.D., D.Sc., M.D., Professor of Pediatrics, Duke University School of Medicine, Durham. (Adaptation of the Title Page of The Compleat Angler by Izaak Walton, 1653.) Third edition. Cloth. Price, $3.75. Pp. 256. Durham, N. C.: Duke University Press, 1940.

This edition of the Compleat Pediatrician will be gratefully received by the many users and admirers of the first two editions. After one has acquired the habit of relying on this practical volume containing in such concise form a wealth of pediatric information as diagnosis, therapeutics, preventive methods, information on feeding diets and nutrition, laboratory tests, and other valuable facts necessary for the pediatrician's armamentariums, each new edition is eagerly received. The present edition has been brought down to date and contains the advances in therapeutics and procedures developed in the past several years; the newer advances in the recognition of vitamin deficiencies and therapeutics are excellently presented, as is the newer knowledge of chemotherapy with special regard to the use of sulfanilamide, sulfapyridine and sulfathiazole. The volume is thin and flexible and should fit into the general practitioner's bag. The younger pediatrician starting to practice will do well to purchase a bag in which this valuable reference book will fit. An experienced pediatrician will find great aid and comfort in frequently referring to the facts in this volume which have slipped from his memory and which can be quickly and accurately referred to in the Compleat Pediatrician.

Cyclopropane Anesthesia. By Benjamin Howard Robbins, B.A., M.S., M.D., Associate Professor of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tenn. Cloth. Price, $3. Pp. 175, with 40 illustrations. Baltimore: Williams & Wilkins Company, 1940.

This book represents a review of the literature on cyclopropane as an anesthetic agent. The physiologic and chemical properties of cyclopropane are presented, as are also the concentrations required for anesthesia based on accurate determinations of the amount of cyclopropane in the patient's blood. The author's results are compared to the results of others. The effect of cyclopropane on the various systems of the body is considered—the circulatory system, with special emphasis on the effect of the agent on the heart, and the effect on the respiratory system, gastrointestinal tract, blood and tissues. The section on the clinical administration of cyclopropane is brief and not as complete as a clinician would wish it to be. Complications are dealt with briefly, as are indications and contraindications. The explosive hazards of cyclopropane are considered briefly. Although common precautions which should be taken when this agent is employed are mentioned, many of the special precautions as they are recognized today are not mentioned. The book is of great interest to the anesthetist because it sets forth the point of view of the pharmacologist and presents data which are not so carefully studied by the clinician as by the laboratory man. The volume is a valuable contribution and should be read by all anesthetists and also those who have to do with the use of cyclopropane as an anesthetic agent.

Dental Caries: Findings and Conclusions on Its Causes and Control Stated in 195 Summaries by Observers and Investigators in Twenty-Five Countries. Compiled for the Research Commission of the American Dental Association by the Advisory Committee on Research in Dental Caries: Daniel F. Lynch, Chairman, Charles F. Kettering, Counselor, William J. Gies, Secretary. Cloth. Price, $1. Pp. 189. New York, 1939.

This is the compilation of 195 summaries from observers and investigators in twenty-five countries followed by a general analysis, presumably by the secretary of the committee. The material for compilation was obtained by circularization of an "open letter to all investigators throughout the world in the field of dental caries" and directed to "each living person who, from research or clinical observation, has published findings and conclusions that bear in any way, directly or indirectly, on the cause or control of dental caries in man or animals." Further in the preface this statement is made: "It was not our purpose to evaluate the findings and conclusions in this book, nor to suggest which views may be regarded as most significant. Presumably, these functions will be performed publicly by reviewers and special students of caries." In spite of this the general analysis is of no little assistance in bringing order out of what would otherwise be a chaotic situation, and a situation which a reviewer could not at all clear up publicly in the space usually allotted to a review. The book serves one useful purpose; namely, and in the language of the committee, "We aimed only to compile the data and to make them readily available for constructive use by those who will promote public discussion, and who will advance further research and clinical inquiry." And again quoting: "The critical reader will be the judge of the relative values of the individual contributions." There is a definite need for such discrimination.

A Textbook of Psychiatry. By Arthur P. Noyes, M.D., Superintendent, Norristown State Hospital, Norristown, Pennsylvania, and Edith M. Haydon, A.B., R.N., Superintendent of Nurses, St. Elizabeths Hospital, Washington, D. C. Third edition. Fabrikoid. Price, $2.50. Pp. 315, New York: Macmillan Company, 1940.

In this edition there are additional data on nursing treatment. A psychiatric nurse collaborated with the senior author in the presentation of the latter material. The book is primarily written for the student nurse and as such fills a great need satisfactorily. There are thirty-three chapters, all dealing with some phase of normal and abnormal behavior. Some of the chapters are written too briefly, even though the book is written for nurses. There is a short but good history of psychiatry and of psychiatric nursing. The book is recommended for student nurses and graduate nurses interested in psychiatry.

Feeding the Family. By Mary Swartz Rose, Ph.D., Professor of Nutrition, Teachers College, Columbia University, New York. Fourth edition. Cloth. Price, $3.75. Pp. 421, with illustrations. New York: Macmillan Company, 1940.

This is one of the most authoritative and reliable books available in the field of nutrition. The numerous editions through which it has passed and its widespread use testify to its value. In her preface, Dr. Rose emphasizes the increased emphasis on the feeding of the child, on the feeding of the mother during the critical antepartum period and the feeding during the first years of life. There is also a discussion of the ideal maintenance diet for the adult. Economic considerations have caused a scrutiny of diets with a view to possible improvement without undue increase in cost. Attention is called also to the new emphasis that has been given to thiamine in recent years. A section on allergy has been added to the chapter on feeding the sick. The book can be unhesitatingly recommended for use as a text, for the physician who needs constantly at hand a reliable work of reference and, indeed, for the general reader.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Sponge Left in Abdomen: Res Ipsa Loquitur.—The physician defendant performed a cesarean section on Mrs. Key. As the patient appeared to be "a poor surgical or anaesthetic risk" it was deemed necessary to complete the operation as quickly as possible. While suturing the incision made in the uterus the physician called for a count of the sponges which he had removed from the field of operation. The nurses who were assisting him made the count and told him that it was correct and he then closed the abdominal incision. He again called for a sponge count and was again informed that the second count was correct. All the sponges used to pack off the field of operation were personally placed by the physician and were removed by him. About five weeks later it was discovered that a sponge, which had been used to prevent the transverse colon from sagging into the field of operation, had been left in the patient's abdomen. The patient and her husband subsequently sued the physician for malpractice, alleging that he had been negligent in allowing the sponge to remain in the patient's abdomen. The trial court, apparently relying on the doctrine of res ipsa loquitur, found, in effect, that the physician had been negligent and the physician appealed to the district court of appeal, second district, division 2, California.

The defendant contended that there was no evidence adduced at the trial to support the finding that he had been negligent. While he conceded that the doctrine of res ipsa loquitur was applicable, he contended that the inference of negligence, which the application of that doctrine would attribute to him, was rebutted by his own uncontradicted testimony that in performing the operation he had followed the usual, ordinary and approved medical practice. He argued that any possible inference of negligence arising from the application of the doctrine of res ipsa loquitur was overcome by the facts that (1) there was no medical expert testimony to any other effect than that he had followed approved medical practice in performing the operation and (2) that what is or is not proper medical practice can be established only by medical expert testimony, which, when not conflicting, is conclusive. Hence, he insisted that there was nothing in the record on which the trial court's finding of negligence could be based. The district court of appeal, however, held to the contrary. It relied for its decision on *Ales* v. *Ryan*, 8 Cal. (2d) 82, 64 P. (2d) 409, in which the Supreme Court of California said:

> . . . the failure to remove a sponge from the abdomen of a patient is negligence of the ordinary type and that it does not involve knowledge of materia medica or surgery but that it belongs to that class of mental lapses which frequently occur in the usual routine of business and commerce, and in the multitude of commonplace affairs which come within the group of ordinary actionable negligence. . . . General negligence cannot be excused on the ground that others in the same locality practice the same kind of negligence.

The physician's testimony, continued the court, that he followed the usual and ordinary practice in performing the operation does not compel a finding that the inference of negligence arising from the fact that he failed to remove one of the sponges was rebutted. The question whether such inference has been rebutted is ordinarily for the determination of the trial court. The court again adverted to *Ales* v. *Ryan*, supra, and noted that it quoted with approval from *Davis* v. *Kerr*, 239 Pa. 351, 86 A. 1007, 46 L. R. A. (N. S.) 611, as follows:

> . . . Here the surgeon had reached the conclusion that he had removed all the sponges—a mistaken conclusion, but verified by the nurses' count. In reaching his conclusion, did he exercise ordinary skill? We see nothing in the evidence to warrant the inference that he did not; but, on the other hand, we find nothing to warrant the inference that he did, which is far more important, since the burden of showing care was upon him. Why was a foreign substance left in the parts, which the operating surgeon should have removed? It was for him to acquit himself of negligence with respect to it. The sponge escaped his observation. Why? Was it so hidden and concealed that reasonable care on his part would not have disclosed it, or were conditions such that, in his professional judgment, further exploration by him for sponges would have endangered the safety of the patient? In a word, did he do all that reasonable care and skill would require? Except as one or the other of these questions can be answered affirmatively from the evidence, the law will presume to the contrary, and attribute the unfortunate consequences to his contributing negligence.

But, continued the district court of appeal, in the instant case there was no evidence that the physician made any attempt by exploration in the patient's abdominal cavity to verify the sponge count which the nurses had announced as correct, nor was it shown that such exploration, if made, would have endangered the patient's safety. It did not appear that the sponge was so concealed that reasonable care on his part would not have disclosed it. On the contrary, the physician's own testimony lent strength to the inference of negligence arising from the application of the doctrine of res ipsa loquitur. His testimony was that the sponge which he had left in the patient's abdominal cavity was of the type used by him in every cesarean operation and was one which he used for the same purpose and placed in the same position in the abdominal cavity. It thus appeared that the sponge in question was of the ordinary type placed as a routine in the same position in every operation, and no compelling explanation was offered for his failure to remove it. The trial court was therefore justified in drawing the inference from the facts proved that the physician did not do all that reasonable care and skill would require.

The physician, continued the court, rested his case entirely on the testimony that in completing the operation as speedily as possible and in relying on the sponge count by the nurses he was following the usual and ordinary practice of other physicians in the same locality. But, a physician cannot relieve himself of liability by proof of a custom or practice among physicians requiring nurses to count the sponges used in an operation. The court concluded that, since the operation in question was performed under his immediate supervision and direction, the defendant physician was charged with the responsibility of determining that all sponges were removed from the field of operation before the incision was closed.

The judgment in favor of the patient and her husband accordingly was affirmed.—*Key et ux. v. Caldwell (Calif.), 104 P. (2d) 87.*

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Oto-Laryngology, Cleveland, Oct. 6-10. Dr. William P. Wherry, 107 South 17th St., Omaha, Secretary.

American Academy of Pediatrics, Memphis, Tenn., Nov. 18-20. Dr. Clifford G. Grulee, 636 Church Street, Evanston, Ill., Secretary.

American Clinical and Climatological Association, White Sulphur Springs, W. Va., Oct. 28-30. Dr. Francis M. Rackemann, 263 Beacon St., Boston, Secretary.

American College of Surgeons, Chicago, Oct. 21-25. Dr. Frederic A. Besley, 40 East Erie St., Chicago, Secretary.

American Public Health Association, Detroit, Oct. 8-11. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.

American Society of Anesthetists, New York, Oct. 10. Dr. Paul M. Wood, 745 Fifth Avenue, New York, Secretary.

American Society of Tropical Medicine, Louisville, Ky., Nov. 12-15. Dr. E. Harold Hinman, Malaria Control Division, Wilson Dam, Ala., Secretary.

Association of Military Surgeons of the United States, Cleveland, Oct. 10-12. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.

Central Society for Clinical Research, Chicago, Nov. 1-2. Dr. Carl V. Moore, Washington University School of Medicine, St. Louis, Secretary.

Clinical Orthopaedic Society, Milwaukee and Madison, Wis., Oct. 18-19. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

District of Columbia, Medical Society of the, Washington, Oct. 15-17. Mr. Theodore Wiprud, 1718 M St., N.W., Washington, Secretary.

Indiana State Medical Association, French Lick, Oct. 29-31. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Inter-State Postgraduate Medical Association of North America, Cleveland, Oct. 14-18. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.

Nevada State Medical Association, Las Vegas, Oct. 11-12. Dr. Horace J. Brown, 120 North Virginia St., Reno, Secretary.

New York State Association of Public Health Laboratories, Albany, Nov. 1. Miss Mary B. Kirkbride, New Scotland Avenue, Albany, Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 28-Nov. 1. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.

Pacific Coast Society of Obstetrics and Gynecology, San Francisco, Nov. 6-9. Dr. T. Floyd Bell, 400 Twenty-Ninth St., Oakland, Calif., Secretary.

Southern Medical Association, Louisville, Ky., Nov. 12-15. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.

Southwestern Medical Association, Tucson, Ariz., Nov. 21-23. Dr. M. P. Spearman, 1001 First National Bank Bldg., El Paso, Texas, Secretary.

Vermont State Medical Society, Rutland, Oct. 9-10. Dr. B. F. Cook, 154 Bellevue Ave., Rutland, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Obstetrics and Gynecology, St. Louis

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*Pregnandiol Determination as Aid in Clinical Diagnosis. C. L. Buxton, New York.—p. 202.
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Tattooing (Puncturation) with Mercury Sulfide for Treatment of Intractable Pruritus Caused by Leukoplakia-Kraurosis Vulvae. R. Turell, New York.—p. 334.

Pregnandiol Determination as Aid in Clinical Diagnosis.—According to Buxton, the determination of the metabolism and excretion of progesterone, the corpus luteum hormone, has heretofore been impossible because there has been no accurate method for measurement of this substance either in the body or as an excretion product. The discovery of pregnandiol and its identification as an excretion product of progesterone has made it possible to determine the presence of progestational activity with a fair degree of accuracy. The metabolism of progesterone to sodium pregnandiol glucuronidate in the body is a complex process. Pregnandiol determinations were done on four women during and following the injection of 30 mg. of progesterone daily for three days. Three of these patients had had a subtotal and one a total hysterectomy. Two of the patients excreted sodium pregnandiol glucuronidate, whereas the other two did not. It has been found that men receiving injections of progesterone excrete large amounts of sodium pregnandiol glucuronidate. The uterus, therefore, is not considered a necessary adjunct to this metabolic process. Its synthesis as sodium pregnandiol probably occurs in the liver. Since the metabolism of progesterone apparently involves a number of factors, an investigation was made of various laboratory animals. It was found that the urine of monkeys, cats and rabbits does not contain pregnandiol either normally, during pregnancy or after progesterone injections. The greatest yield and purest form of pregnandiol glucuronidate occurs in the urine of pregnancy. No pregnant women have been observed who do not excrete pregnandiol glucuronidate. Therefore negative diagnosis of pregnancy may be made from a negative pregnandiol determination. Pregnandiol is present in small amounts in the urine of normal women during the latter half of the menstrual cycle. Although the excretion during pregnancy is greater than that during the luteal phase of the menstrual cycle, a diagnosis of pregnancy cannot be made on this basis because the quantitative determination is not sufficiently accurate. Five cases of habitual abortion were tested for pregnandiol excretion during subsequent pregnancies. One of these patients aborted spontaneously during the course of progesterone therapy. She showed unusually low pregnandiol excretion. Seventy-eight simultaneous pregnandiol determinations and endometrial biopsies were done on patients, most of whom were in the sterility clinic. These tests were done in order to ascertain the accuracy of these two methods of determining progestational activity. It is apparent that pregnandiol is excreted during the time that the endometrium is being activated to a secretory phase and only during that time. There are so many factors controlling the excretion of pregnandiol glucuronidate that the quantitative result is liable to variation. Therefore diagnosis cannot be made on a basis of quantitative differences in excretion.

Evaluation of Stilbestrol as Therapeutic Estrogen.—According to Salmon and his associates, numerous clinical reports attested the fact that, in human beings, stilbestrol was capable of relieving menopausal symptoms. The authors studied the biologic and therapeutic effects of stilbestrol in forty-five cases. The investigations included the effect on the vaginal smear, vaginal mucosa and endometrium, the capacity of the substance to inhibit the excessive gonadotropic hormone excretion in the menopausal patient and its effectiveness in relieving the menopausal symptoms. The studies revealed that stilbestrol has an estrogen-like effect on the human vaginal mucous membrane and endometrium; that if sufficient stilbestrol is administered it appears to inhibit the excessive excretion of gonadotropic substance in the menopause. Stilbestrol relieves the hot flushes of the menopause but it does not impart to the patient the feeling of well-being and relief from nervous instability that usually result from treatment with the natural estrogens. Toxic symptoms were observed in 64 per cent of the forty-five patients. The toxic symptoms most commonly noted were nausea, vomiting and vertigo. The authors are of the opinion that the high incidence of toxic symptoms militates against the usefulness of stilbestrol as a therapeutic agent.

American Journal of Ophthalmology, St. Louis

23:853-970 (Aug.) 1940

Concerning the Chamber Angle: I. Gonioscopy. H. S. Sugar, Chicago.—p. 853.
Hyperuricemia and Inflammations of Eye. H. C. Kluever, Fort Dodge, Iowa.—p. 867.
Historical Notes on Ophthalmoscopy. E. Jackson, Denver.—p. 873.
Transplantation of Cornea by Means of a Mechanically Obtained Beveled-Edge Segment. M. Wiener and B. Y. Alvis, St. Louis.—p. 877.
Projection Method of Presenting Test Object for Testing Visual Acuity. C. E. Ferree and G. Rand, Baltimore.—p. 882.
Binocular Anomalies and Reading Ability. B. Clark, San Jose, Calif.—p. 885.
Metastatic Carcinoma of Choroid with Primary Focus in Prostate Gland. M. M. Kulvin, Chicago.—p. 892.
A Clinician's Experience with Sulfanilamide. B. Chance, Philadelphia.—p. 900.
Some Interesting Muscle Cases with Comments. R. O'Connor, San Francisco.—p. 904.
Blood Differential Count in Chronic Glaucoma. E. M. Blake and J. C. Leonard, New Haven, Conn.—p. 907.
*Local Use of Sulfanilamide in Trachoma: Preliminary Report. K. W. Cosgrove, Little Rock, Ark.—p. 911.

Local Use of Sulfanilamide in Trachoma.—According to Cosgrove, 206 cases of trachoma have been diagnosed and treated by clinics held in the northwest and northern parts of Arkansas. The patients (ninety-seven) with no apparent physical disability which would contraindicate oral administration of sulfanilamide were given 20 grains (1.3 Gm.) of the drug daily to an adult male, 15 grains (1 Gm.) to an adult female and 10 grains (0.065 Gm.) to a child. In addition an 0.8 per cent solution of sulfanilamide was given to the patient to be dropped into the eyes from four to six times a day. The patients who were not considered good risks for oral treatment were given only the local treatment. Patients were instructed to cleanse the eyes with warm water every morning and evening. No other medication was used. All the patients reported a cessation of lacrimation and photophobia within the first three days. Sixty-three

patients who received oral medication were reexamined and questioned regarding undesirable symptoms. At least thirteen patients discontinued the oral medication, thus increasing the number of those who in reality received only local treatment. No discomfort was reported by these patients. Improvement in visual acuity among patients given oral and local medication indicates that 46 per cent had a visual acuity of 20/70 or better, and 19 per cent were improved to 20/30 or better. Of the patients who received only local treatment 62 per cent had a visual acuity of better than 20/70 and 31 per cent improved to 20/30 vision or better. The trachoma of the two groups of patients was similar; thus the greater percentage of improvement with local medication was not influenced by the stage of trachoma. It is probable that in a larger number of cases the percentages would have been more nearly equal. Thus the symptomatic relief of the patient with trachoma on local sulfanilamide is apparently as rapid and complete as that obtained from oral medication. The results also reveal that small doses of sulfanilamide supplemented by local application can be used in ambulatory clinics with the same results as are obtained from large doses. The author suggests that it may be possible to prevent the recurrence of trachoma after sulfanilamide therapy by its continued local use with no danger to the patient's health.

American Journal of Psychiatry, New York

97:1-254 (July) 1940

Organization and Administration in Psychiatry. W. C. Sandy, Harrisburg, Pa.—p. 1.
Study of 100 Patients Suffering from Psychosis with Cerebral Arteriosclerosis. H. E. Clow, White Plains, N. Y.—p. 16.
Respiratory Response of Psychoneurotic Patients to Ideational and to Sensory Stimuli: Respiratory Response in Psychoneuroses. J. E. Finesinger and Sarah G. Mazick, Boston.—p. 27.
Intracranial Tumors in Mental Hospital Patients: Statistical Study. C. P. Larson, Fort Steilacoom, Wash.—p. 49.
Pharmacologic Shock Treatment of Schizophrenia: Statistical Study of Results in the Ohio State Hospitals. J. F. Bateman and N. Michael, Columbus, Ohio.—p. 59.
Psychiatric Findings in Cases of 500 Traffic Offenders and Accident-Prone Drivers. L. S. Selling, Detroit.—p. 68.
*Survey of Mental Illness Associated with Pregnancy and Childbirth. J. L. Smalldon, White Plains, N. Y.—p. 80.
Dynamic Disturbances in the Handwriting of Psychotics, with Reference to Schizophrenic, Paranoid and Manic-Depressive Psychosis. Thea Stein Lewinson, New York.—p. 102.
Treatment of Delirium Tremens with Insulin in Subshock Doses. G. W. Robinson Jr., Kansas City, Mo.—p. 136.
Study of Insight of Psychiatric Patients. C. W. Osgood, Wauwatosa, Wis.—p. 152.
Effect of 10 Mg. of Benzedrine Sulfate on Otis Test Scores of College Students. J. E. Barmack, New York.—p. 163.
Prognostic Criteria in Dementia Paralytica. M. H. Greenhill and M. Yorshis, Worcester, Mass.—p. 167.
Comparative Study of Thinking in Schizophrenic Children and in Children of Preschool Age. J. Louise Despert, New York.—p. 189.
Set in Schizophrenic as Measured by Composite Reaction Time Index. E. H. Rodnick and D. Shakow, Worcester, Mass.—p. 214.

Psychoses in Pregnancy and Childbirth.—Smalldon studied the records of 220 women admitted to the New York Hospital, Westchester Division, because of mental illness associated with childbirth and the puerperium. These cases comprised roughly 8 per cent of the female admissions during the period (1922 to 1938) under study. This coincides with certain other published data. Williams has stated that only one in 1,000 women are so affected during pregnancy or childbirth. Manic-depressive psychoses accounted for 107 of the cases, dementia praecox for sixty-four, psychoneurosis for twenty-eight, psychosis with a psychopathic personality for ten, toxic-exhaustive psychosis for eight, a psychopathic personality with pathologic emotionality but without psychosis for two and a paranoid condition for one. Contrary to other reports, only 3.6 per cent of the cases were classified as deliriums directly attributed to the toxic-exhaustive factors of reproduction, although such factors were frequently precipitating causes in the development of rather typical manic-depressive reactions, particularly of the depressive type. Probably this difference in diagnosis may be attributed to the increasing recent tendency away from the belief that a specific psychosis occurs in the pregnant and postpartum states and toward the conception that the physical and psychic problems of childbirth do not determine the type of psychosis but merely act as exciting or precipitating agents. This is particularly attested by the fact that most of the toxic-exhaustive cases were so diagnosed in the first half of the period under study. Further, a variance of many of the previously reported dynamic factors was found, emphasizing the difficulty of generalization regarding the mechanisms of these reactions. Undoubtedly the psychoanalytic explanations given of certain cases are quite correct but the author wonders whether one can postulate from these cases that other similar cases develop from a similar set of circumstances and by means of the same dynamics. It seems to him that each case of postpartum illness must be considered as an individual, nongeneralizable problem. His study does not corroborate the fact that a high proportion of the depressive type of manic-depressive psychoses and puerperal schizophrenias are of paranoid reaction. It rather shows a greater percentage of catatonia. The study corroborates the observations of Strecker and Ebaugh that these schizophrenic reactions frequently show pronounced manic-depressive symptoms, clouding of the sensorium and a tendency to remissions, that these cases tend to slow deterioration and that a high percentage of postpartum psychoses occur in the Jewish race. The slow deterioration may be due to the predominance of catatonic types rather than to a modification of the schizophrenic process by the reproductive process. The study shows a considerably greater morbidity in the heredity of the manic-depressive group than in the schizophrenic and toxic-exhaustive groups, and a still greater morbidity in the heredity of the psychoneurotic and psychosis with psychopathic personality groups. Many personality deviations were not observed. A high percentage of incest and homosexual ideas, considered by Zilboorg to be typical of puerperal depressive reactions, was not found. Likewise contrary to his claim a slightly greater number showed a mother preference. The study tends to corroborate to some degree Zilboorg's claim that the aloof, shy woman with little previous contact with men and prolonged courtship tends to develop puerperal schizophrenia. Antagonism toward the child, as expected from Zilboorg's hypothesis, was present. With few exceptions the psychoses did have their onset post partum. The schizophrenias reported by Zilboorg developed predominantly in multiparas, while those of the present series were slightly more frequent in primiparas. His assumption of the masculine role in the interval between pregnancies was lacking. A sense of guilt was found more frequently than by Zilboorg.

American Journal of Tropical Medicine, Baltimore

20:463-624 (July) 1940

Rickettsia Diaporica and American Q Fever. H. R. Cox, Hamilton, Mont.—p. 463.
Neurotropic Virus Isolated from Blood of Native of Uganda. K. C. Smithburn, T. P. Hughes, A. W. Burke and J. H. Paul, Entebbe, Uganda.—p. 471.
*Results of Recent Studies of Hookworm in Eight Southern States. A. E. Keller, W. S. Leathers and P. M. Densen, Nashville, Tenn.—p. 493.
Echinostoma Lindoensis N. Sp., a New Parasite of Man in Celebes, with an Account of Its Life History and Epidemiology. J. H. Sandground, Indianapolis, and C. Bonne, Batavia, Java.—p. 511.
Preliminary Report on Practical Epidemiology and Control of Endemic Typhus Fever in Georgia. C. D. Bowdoin and R. J. Boston, Atlanta, Ga.—p. 537.
Falciparum Malaria in Drug Addicts: Clinical Aspects. H. Most, New York.—p. 551.
Oviposition Experiments with Anopheline Mosquitoes. M. Bates.—p. 569.
Comparative Evaluation of Paris Green and Pyrethrum Emulsion as Anopheline Larvicides in Georgia: Progress Report. J. M. Henderson and R. S. Howard Jr.—p. 585.
Importance of Recognizing Secondary Vitamin Deficiencies. Susan Gower Smith, Durham, N. C.—p. 593.

Hookworm in Southern States.—Keller and his associates present data on the incidence of hookworm in the Southern states in which a plan of control was instituted by the Rockefeller Sanitary Commission in cooperation with the state departments of health. Hookworm surveys were made in eight Southern states during the periods 1910-1914 and 1930-1938. In the early period 577,590 specimens of feces were examined, and in the later period 424,511. The numbers found positive in the early and later periods were 240,895 and 81,913 respectively. After adjustment for the distribution of the population the percentage found positive in six of the eight states was 36.6 in the earlier period and 11.2 in the later period, resulting in a reduction of 68.3 per cent. In the later study the states in the order

of prevalence from highest to lowest were Mississippi, South Carolina, Alabama, North Carolina, Kentucky and Tennessee. While there is a widespread distribution of hookworm, the areas of highest incidence are confined to the coastal plain and sandy soil areas of each state. The age distribution shows that the greatest prevalence was in the group 5 to 19 years of age. The peak of incidence, 24.5 per cent, was reached in the age period 15 to 19. In preschool children and adults the incidence was about half as great as that found in the school age group. The distribution of all positive cases shows that about one fourth of the individuals had moderate, heavy or very heavy worm infestations sufficiently severe to produce clinical symptoms. The remainder of the cases were classified as very light or light infestations. The data analyzed with reference to household groups seemed to indicate that the individual worm burden tended to increase as the number of infested persons in the family increased. A comparison was made of hookworm in 17,458 Negroes and 59,028 white persons in the same counties during 1930-1938. The incidence in Negroes was about one fourth that in white individuals and the average intensity of infestation was about one half that found in white persons.

Annals of Surgery, Philadelphia

112:161-320 (Aug.) 1940

Tumors of Islet Cells with Hyperinsulinism; Benign, Malignant and Questionable. V. K. Frantz, New York.—p. 161.
Acute Pancreatitis and Diabetes. H. B. Shumacker Jr., Baltimore.—p. 177.
*Indications for Lobectomy and Pneumonectomy in Pulmonary Tuberculosis. P. C. Samson, Oakland, Calif.—p. 201.
Injections of Air and of Carbon Dioxide into Pulmonary Vein. R. M. Moore and C. W. Braselton Jr., Galveston, Texas.—p. 212.
Conservative Electrosurgical Excision of Subesophageal, Chronic Penetrating or Acutely Perforated Gastric Ulcer: Report of Unusual Case Thus Treated—with Good End Results. R. H. Jackson, Madison, Wis.—p. 219.
*Tuberculosis of Stomach: Clinical and Pathologic Study. R. C. Sullivan, N. T. Francona and J. D. Kirshbaum, Chicago.—p. 225.
Ladd's Operation for Cure of Incomplete Rotation and Volvulus of Small Intestine Producing Duodenal Obstruction in Infancy. R. Elman, St. Louis.—p. 234.
Plasma Transfusion in Experimental Intestinal Obstruction. J. Fine, Boston, and S. Gendel, Los Angeles.—p. 240.
Metastatic Pulsating Tumor of Bone Secondary to Renal Carcinoma: Case Report. H. E. Shih and S. H. Wang, Peiping, China.—p. 249.
Delayed Closure of Contaminated Wounds: Preliminary Report. F. A. Coller and W. L. Valk, Ann Arbor, Mich.—p. 256.
Operative and Postoperative Infections, with Special Reference to Air-Borne Bacterial Contamination. W. Walters and T. B. Magath, Rochester, Minn.—p. 271.
Wound Infection: Comparison of Silk and Catgut Sutures. D. C. Elkin, Atlanta, Ga.—p. 280.
Graduate Teaching of Surgical Pathology. A. P. Stout, New York.—p. 284.

Indications for Lobectomy and Pneumonectomy for Tuberculosis.—Samson discusses indications and contraindications to lobectomy and pneumonectomy in tuberculosis and reports three instances of each. The appreciation of tuberculous bronchial stenosis with its resultant pulmonary atelectasis has followed the increasing use of the bronchoscope in cases of pulmonary tuberculosis. This type of case, which is not uncommon, refutes the belief that pulmonary atelectasis is a favorable prognostic sign in tuberculosis. Most of these patients cannot become entirely and permanently well without surgery. Indications for lobectomy differ from those for pneumonectomy. Stenosis of the lobar bronchus was not a factor in the three cases of lobectomy. The position of the cavity was important. Their presence in the lower and middle lobes indicated lobectomy and made the effectiveness of thoracoplasty doubtful. Pulmonary resection carries a greater risk than thoracoplasty. In cases in which thoracoplasty is not suitable and in those in which it has been performed without cure lobectomy may be indicated. The tuberculosis should be sharply limited to the portion of the lung to be resected. Lobectomy and pneumonectomy may be primary or secondary procedures. In the latter are those cases of pulmonary resection designed to remove cavity-bearing pulmonary tissue which has not been collapsed by a technically adequate thoracoplasty. The advisability of removing a lobe in which a cavity has not been collapsed by a pneumothorax is probably unwise without first obliterating the interpleural space by thoracoplasty. Planned pulmonary resection, not preceded by thoracoplasty, may be listed as a primary procedure. Pneumonectomy should be considered for patients with total atelectasis of one lung and advanced fibrous stenosis of the stem bronchus who occasionally suffer from obstructive symptoms not relieved by bouginage of the stricture. Pneumonectomy probably should be deferred until mucosal healing and fibrostenosis have occurred in cases in which bronchial obstruction is due primarily to extensive ulcerative disease. A large isolated cavity in a lower or middle lobe is the first indication for primary lobectomy. The decision is strengthened by the presence of concomitant atelectasis and bronchiectasis or by a stenotic lobar bronchus. Obviously pneumothorax, phrenic paralysis and pneumoperitoneum, or a combination of these procedures, will have been tried prior to considering lobectomy. Repeated severe hemorrhages from a tuberculous cavity is a further indication.

Tuberculosis of Stomach.—According to Sullivan and his associates, from 1929 to 1938 in 11,480 consecutive necropsies performed at the Cook County Hospital there were 288 cases of pulmonary tuberculosis and in 242 additional cases pulmonary tuberculosis was found incidentally, death occurring from some other unrelated cause. There was one instance of tuberculosis of the stomach encountered in the former group of cases. In a third group of twenty-four cases in which a generalized tuberculous adenopathy was the primary cause of death, one case of tuberculosis of the stomach was present. Thus in 554 cases of tuberculosis the stomach was involved in two cases, while during the same time only one case was encountered in 75,000 surgical specimens. Pathologically, two types of tuberculosis of the stomach are to be discerned: 1. Miliary tuberculosis, in which the stomach contains single caseous tubercles which are located in the submucosa or on the serosa and are a part of the stage of generalization. 2. Ulcerative tuberculosis, which is characterized by numerous shallow, irregularly shaped ulcers with overhanging margins and grayish yellow bases, which rarely penetrate the muscular layer. They may eventually cause scarring and shrinking of the stomach, simulating syphilis or carcinoma. The sources of infection are thought to be direct invasion of the mucosa through the blood stream or lymph or by direct extension. Two of the cases were of the ulcerative type. The case of a 34 year old Negro with tuberculosis localized to the stomach and perigastric lymph nodes is described. Gastric resection has thus far completely eradicated the disease. Epithelioid cell tubercles were present in the gastric wall and in the perigastric lymph nodes. This type of case is of interest to the gastroenterologist and the surgeon in view of the diagnostic problem that it presents. The differential diagnosis usually considered is carcinoma or syphilis of the stomach, and tuberculosis is practically never included. Even the gross examination of the excised segment of the stomach resembles a malignant condition. The correct diagnosis is not suspected until microscopic examination is made. The prognosis is usually good following surgery in cases in which the general condition is fairly good and when there are no signs of active tuberculosis elsewhere in the body. The earliest symptoms are not characteristic. They are usually those of chronic gastritis with loss of appetite and a sense of fulness or pressure in the epigastrium. This is followed by epigastric distress or pain of the ulcer type, loss of weight and vomiting. The vomiting occurs late in the disease and the vomitus is dark or suggestive of gastric hemorrhage.

Archives of Otolaryngology, Chicago

32:195-416 (Aug.) 1940

Innocuous Oils Useful in Rhinologic Practice, in Contrast to Liquid Petrolatum. F. J. Novak Jr., Chicago.—p. 195.
Benign and Malignant Tumors of Jaw. F. R. Spencer, Boulder, Colo.; C. F. Hegner and W. C. Black, Denver.—p. 200.
Role of Sulfanilamide in Treatment of Acute Otitis Media. J. W. Babcock, New York.—p. 246.
Surgical Treatment and Its Complications in Cases of Acute Sinusitis. W. L. Simpson, Memphis, Tenn.—p. 250.
Intradural Conditions in Relation to Rhinology and Otology: Critical Survey of Recent Literature. W. P. Eagleton, Newark, N. J.—p. 256.
Teaching the Laryngectomized Patient to Talk (Without Aid of Mechanical Larynx). N. M. Levin, Philadelphia.—p. 299.
Sarcoidosis of Larynx. D. L. Poe, New York.—p. 315.
Treatment of Acute Laryngotracheobronchitis. F. W. Davison, Danville, Pa.—p. 321.
Paranasal Sinuses. S. Salinger, Chicago.—p. 341.

Archives of Physical Therapy, Chicago

21:449-512 (Aug.) 1940

Diathermy in Ophthalmology. A. D. Ruedemann and W. J. Zeiter, Cleveland.—p. 451.
Orthopedic Gymnastic Treatment of Spinal Abnormalities. H. G. Hadley, Washington, D. C.—p. 455.
Electrosurgery of Brain and Spinal Cord. J. G. Lyerly, Jacksonville, Fla.—p. 459.
Colonic Irrigation: Indications and Technic. W. Cline, Miami, Fla.—p. 465.
Simple Device for Forced Flexion of Knee. E. C. Elkins, Rochester, Minn.—p. 468.
Esophageal Dysfunction Treated with Sinusoidal Current. M. J. Mandelbaum, New York.—p. 470.
Roentgen Therapy in Otorhinology. M. S. Ersner, Philadelphia.—p. 477.
Therapeutic Advances in Vasomotor Rhinitis and Bronchial Asthma. J. A. Haiman, New York.—p. 486.
Detachment of Retina: End Results of Electrosurgical Treatment. H. S. McKeown, New York.—p. 489.

California and Western Medicine, San Francisco

53:53-104 (Aug.) 1940

Gas Changes in Maternal and Fetal Blood During Cyclopropane Obstetric Anesthesia. E. A. Rovenstine, J. Adriani and W. E. Studdiford, New York.—p. 59.
Amputation Through Lower Third of Femur: Modified Technic. C. E. Rees, San Diego.—p. 64.
Dissecting Aneurysm. E. S. Kilgore, San Francisco.—p. 66.
Some Aspects of Nutrition in Surgical Patients. I. S. Ravdin, Philadelphia.—p. 68.
History of Anesthetic Department at Lane Stanford University Hospital in San Francisco. Adena C. Dutton, San Francisco.—p. 70.
Early Care of Severe Thermal Injuries. H. McCorkle, San Francisco.—p. 72.
*Obstetric Complications: Major Complications Encountered in 10,708 Obstetric Cases in the University of California Hospital. P. L. Martin, San Francisco.—p. 74.
Discussion Groups as an Adjunct to Psychotherapy. M. R. Somers and Pearl S. Pouppirt, San Francisco.—p. 79.

Obstetric Complications.—Martin studied the obstetric complications which occurred in 4,928 deliveries between 1916 and 1926 and the 5,780 encountered between 1927 and 1937. Pelvic contraction was found in only 187 cases, or 1.75 per cent of the total series. The problem of difficult labor is summarized as follows: The choice of a method of delivery for any given case is never complete without considering the pelvis, position, size of the baby, character of the pains and condition of the soft tissues. The risk to the mother and the child is significantly increased when one factor is unfavorable but is greatly increased when two or more factors are unfavorable. The incidence of cesarean operations in the 1927 to 1937 series of cases has doubled, yet there has been but one death in 278 cases, or 0.36 per cent. The aim is to deliver by low cesarean section women on whom high forceps was used formerly. Low or perineal forceps were used in 8.7 per cent of the total material. No insignificant increase in morbidity, mortality or fetal mortality was associated with this procedure. Mid forceps is limited to compelling indications, usually maternal. High forceps performed in the first series was attended with a 7.4 maternal and a 38 per cent fetal mortality. The incidence of mid forceps has changed but little and still is attended with a high fetal mortality. Delivery by version and extraction has been used in only thirty-eight of the 10,708 cases, and then only when indications for immediate delivery were compelling. Two maternal deaths followed, both in relatively desperate cases. An incidence of 3.48 per cent, or 368 breech deliveries, was conducted without maternal mortality but with an uncorrected gross fetal mortality of 12.3 per cent. All antenatal fetal deaths, macerated fetuses and neonatal deaths due to prematurity were included in this percentage. Toxemia of pregnancy developed in 481, or 4.5 per cent, of the total patients; a hypertension of more than 150/100, along with varying degrees of albuminuria and edema, was present. There were thirty-three other cases of convulsive toxemia or eclampsia. There were four maternal and thirty-seven fetal deaths among the 481 nonconvulsive toxemias. There were no maternal deaths and five fetal deaths among the eclamptic patients. All the fetal deaths were of premature infants. One hundred and twenty-two patients of the total series had complicating organic heart disease and were allowed to reach the stage of viability. There were six maternal deaths, or 4.9 per cent mortality. Twenty-four other women were considered too poor risks from the cardiac standpoint and their pregnancies were terminated by therapeutic abortion. Sixteen of the 122 became decompensated during late pregnancy and the six maternal deaths occurred among the decompensated cases. Since 1928 such patients have been followed both by a cardiologist and by an obstetrician and the mortality rate has been strikingly reduced; but one death has occurred since 1928. Pregnancy was complicated by diabetes mellitus in twenty-one cases. One maternal death occurred in the preinsulin days, a patient with severe diabetes who died undelivered of a premature infant while in diabetic coma. There were four fetal deaths. Fibroids have not been a particularly serious complication, as there were few cases with large fibroids. An estimated postpartum blood loss of 600 or more cubic centimeters has been recorded in 230 cases. Ninety-eight of the hemorrhages followed an operative delivery. The exact cause of antenatal bleeding was difficult to determine. However, in sixty-seven cases it was of significant amount and was definitely due to premature separation of a normally implanted placenta and in forty it was due to placenta praevia. Among these 107 cases, twenty cesarean sections were performed. In recent years no manipulations or vaginal examinations were carried out in such cases until cross-matched donors were available and preparations for immediate laparotomy were complete. Probably as a result of such precaution and other improvements in postoperative care there has been but one maternal death in the 1927 to 1937 series. There were six deaths during the 1916 to 1926 series. The author points out that conservatism in obstetric management remains the policy of choice, as is evidenced by the 0.21 per cent uncorrected maternal mortality and the 3.6 per cent uncorrected and 1.8 per cent corrected fetal mortality obtained in the 5,780 deliveries seen between 1927 and 1937.

Canadian Medical Association Journal, Montreal

43:99-200 (Aug.) 1940

*Experience with Pfeiffer Crystallization Method for Diagnosis of Cancer. O. C. Gruner, Montreal.—p. 99.
Treatment of Infiltrating Tumors of Bladder. R. Pearse and R. A. McComb, Toronto.—p. 106.
Recurrent Subarachnoid Hemorrhage Due to Arterial Angioma of Cerebellum and Brain Stem. J. C. Richardson and A. W. Bagnall, Toronto.—p. 111.
Abdominal Aortic Mycotic Dissecting Aneurysm. S. W. Lippincott, Montreal.—p. 115.
Primary Carcinoma of Fallopian Tube. H. A. Baron, Montreal.—p. 118.
Traveling Clinics in Manitoba. A. L. Paine, Ninette.—p. 122.
Corrosion of Metals in Tissues and Introduction to Tantalum. G. L. Burke, Vancouver, B. C.—p. 125.
Effect of Olive Oil and Cod Liver Oil on Gastric Secretion in Dog. Olga Komarov and S. A. Komarov, Montreal.—p. 129.
Progressive Postoperative Gangrene of Skin. I. H. Brodie and C. Bouck, Calgary, Alta.—p. 133.
Genetic Research in Medical Practice. D. de F. Bauer, Montreal.—p. 135.
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Sonne Dysentery In and Around Vancouver. R. Wilson, Vancouver, B. C.—p. 144.
Injury of Urethra in Male Child. R. M. Wansbrough, Toronto.—p. 147.
Colles' Fracture. A. W. M. White, Toronto.—p. 148.
Brill's Disease: Case. J. E. Nichol, Toronto.—p. 151.
Fracture of First Metacarpal Bone. E. S. James and A. Gibson, Winnipeg, Man.—p. 153.
Tetania Parathyropriva: Report of Case. H. H. McGarry, Niagara Falls, Ont.—p. 155.
Treatment of Convulsions with Dilantin Sodium. W. A. Hawke, Toronto.—p. 157.
Appendix Vermiformis Duplex. D. E. Robertson, Toronto.—p. 159.
Pathology of Dissecting Room. C. R. Salsbury, Kingston, Ont.—p. 161.
Note on Histamine. C. H. Best and E. W. McHenry, Toronto.—p. 163.

Pfeiffer's Crystallization Method for Diagnosis of Cancer.—Gruner points out that the patterns which crystals assume after the addition of blood to a solution of cupric chloride have been claimed by E. Pfeiffer to be distinctive between health and disease. The pattern characteristic for cancer has been defined by Pfeiffer as built up on a straight line to the center of which impinge a few lines at angles varying from 5 to 30 degrees. Lines at similar angles may meet at the same point from the opposite side of the base line. The two groups of lines together give an appearance recalling that of tyrosine crystals seen under the microscope. The more numerous and the better defined the groupings in a plate, the more advanced is the case considered to be. The fact that cancerous blood really produces differences which are uniform in kind is readily established even with a few dozen tests. The author performed the crystallization on 122 patients in whom the existence of cancer had been proved, on twenty

cancer patients who had been treated, on thirty-three patients without cancer and on a considerable number of normal and tumor-bearing animals. In Pfeiffer's technic one drop of blood is allowed to fall directly from a finger prick into 1 cc. of distilled water. After thirty minutes two drops (0.1 cc.) of this are introduced into 10 cc. of a 20 per cent cupric chloride. After one-half minute the mixture is poured out on specially prepared plates resting in a specially constructed chamber, and the readings are made after eighteen hours. The only innovation which Gruner has made has been the use of polarized light for reading the slides. The results of the crystallizations done with material obtained from the Royal Victoria Hospital in Montreal are recorded in tables which reveal that the crystallization method gave positive results in 110 of the 122 proved cancer patients; the readings were correct in 90.1 per cent of the cancer cases. In the thirty-three patients without cancer, one positive result was obtained; the percentage of correctness was 96.9 per cent. A positive crystallization test may become negative after excision of the cancer or after treatment by radium. Of the twenty treated cases tested by the author, eleven (55 per cent) were negative. Of animals, those which showed spontaneous tumors or had received grafts showed a positive picture in 79 per cent. Eighteen of twenty-two animals in which the graft did not take gave a negative picture. Eight normal animals of forty-five gave a positive picture and these were mice belonging to a cancer-susceptible strain. A positive crystallization need not necessarily be dismissed as wrong, because the clinician cannot find the tumor. On the contrary, if the test is repeatedly positive the patient should be watched carefully.

Endocrinology, Los Angeles

27:161-344 (Aug.) 1940. **Partial Index**

Review of Experimental and Clinical Trials of Stilbestrol. Dorothy W. Atkinson, San Francisco.—p. 161.
Problem of Hormone Distribution as Controlled by Tissue Uptake. R. Kurzrok and L. Wilson, New York.—p. 166.
Urinary Excretion of Pregnandiol Complex by Males. E. C. Hamblen, W. K. Cuyler and D. V. Hirst, Durham, N. C.—p. 169.
Effect of Testosterone Propionate on Skeletal Development of a Eunuch. I. Rapfogel, New York.—p. 179.
Diagnostic Significance of Cranial Roentgenograms in Pituitary Disease. M. A. Goldzieher, New York.—p. 185.
Diabetes Insipidus of Over Twenty Years' Standing Improved Following Subarachnoid Hemorrhage. S. A. Loewenberg and N. G. Sloane, Philadelphia.—p. 191.
Spontaneous Hypoglycemia in Simmonds' Disease. E. Mogensen, Copenhagen, Denmark.—p. 194.
Epilepsy Complicated by Uncontrollable Diabetes Mellitus. A. T. Ross and W. W. Dickerson, Wahjamega, Mich.—p. 200.
Effects of Hypophysial Stalk Resection on Hypophysis and Hypothalamus of Man. A. T. Rasmussen, Minneapolis, and W. J. Gardner, Cleveland.—p. 219.
Cyclic Changes in Exteriorized Uterus. G. Van Wagenen and A. H. Morse, New Haven, Conn.—p. 268.
Experimental Superfecundity with Pituitary Gonadotropins. H. M. Evans and Miriam E. Simpson, Berkeley, Calif.—p. 305.
Sugar Utilization of Hypophysectomized Rabbits. P. O. Greeley, Los Angeles.—p. 317.
Effect of Anterior Pituitary-like Sex Hormone and Castration on Experimental Tuberculosis. C. B. Brack and L. A. Gray.—p. 322.
Influence of Growth Promoting Hormone of Anterior Lobe of Pituitary on Growth Activity in Long Bones of Rat. Evelyn S. Ross and F. C. McLean, Chicago.—p. 329.

Illinois Medical Journal, Chicago

78:97-192 (Aug.) 1940. **Partial Index**

Role of Kidney in Cardiovascular-Renal Disease. L. G. Rowntree, Philadelphia.—p. 109.
Socialized Medicine. R. C. Berry, Livingston.—p. 128.
Varicose Veins. A. M. Vaughn, Chicago.—p. 137.
Use of Bee Venom in Treatment of Neuritis and Arthritis. B. E. Montgomery, Harrisburg.—p. 148.
Constipation. M. G. Spiesman, Chicago.—p. 153.
Deleterious Effects of Sulfanilamide and Sulfapyridine: Case Report of Agranulocytosis. L. T. Hoyt, Roseville.—p. 161.
Tuberculosis: Home Treatment. H. G. Horstman, Murphysboro.—p. 166.
Peritonsillar Edema in Diphtheria: Danger of Incision. W. M. Youngerman, Champaign.—p. 169.
Trachoma and Follicular Conjunctivitis. M. Hirschfelder, Harrisburg.—p. 171.
An Eye for a Tooth or a Tooth for an Eye. J. E. Lebensohn, Chicago.—p. 174.
Management of Gastrointestinal Disease in Pulmonary Tuberculosis. E. F. Traut, Oak Park.—p. 176.
Treatment of Gonorrhea with New Sulfanilamide Derivative. G. C. Hunt, Springfield.—p. 183.

Journal of Lab. and Clinical Medicine, St. Louis

25:1125-1234 (Aug.) 1940

Experimental Study of Effects of Sulfapyridine on Staphylococci and Staphylococcus Toxin. R. H. Rigdon and P. R. Freeman, Memphis, Tenn.—p. 1125.
Action of Digitaloid Glucosides on Vasomotor Center. P. Blickensdorfer and H. A. McGuigan, Chicago.—p. 1134.
*Quantitative Prothrombin and Hippuric Acid Determinations as Sensitive Reflectors of Liver Damage in Human Subjects. S. J. Wilson, Columbus, Ohio.—p. 1139.
Review of Advances in Study of Auricular Disorders. A. Luisada, Boston.—p. 1146.
Micromethod for Determination of Tissue Lipids. E. L. Outhouse and J. C. Forbes, Richmond, Va.—p. 1157.
Fatal Reactions to Administration of Sulfonamide Drugs: Report of Five Cases. L. J. Tragerman and J. M. Goto, Los Angeles.—p. 1163.
Nutrition and Nervous Excitability. L. Marks and H. Necheles, Chicago.—p. 1177.
Intravenous Administration of Sucrose Solutions as Means of Producing Intense Diuresis. H. F. Helmholz and J. L. Bollman, Rochester, Minn.—p. 1180.
Interrelation Between Vitamin B Complex and Anterior Lobe of Pituitary Gland. D. C. Sutton and J. Ashworth, Chicago.—p. 1188.

Tests for Hepatic Damage.—Wilson found that in forty-one patients without obstructive jaundice or biliary fistulas the quantitative level of the plasma prothrombin correlated closely with the quantity of hippuric acid excreted. In addition to normal individuals the study included persons with cirrhosis of the liver, Banti's syndrome, familial hemolytic icterus, pernicious anemia, aplastic anemia, multiple myeloma, polycythemia vera, Hodgkin's disease and leukemia of all types with various degrees of hepatic infiltration. Among those individuals with proved hepatic damage in which the hippuric acid excretion was between 0.86 and 2 Gm. the prothrombin was found to be between 19 and 37 per cent of normal; with from 2 to 3.9 Gm. of hippuric acid excretion the prothrombin level was between 33 and 90 per cent of normal, and with from 3.9 to 4.56 Gm. of hippuric acid excretion the prothrombin level was between 70 and 100 per cent of normal. No consistent correlation was noticed between plasma prothrombin and plasma fibrinogen, particularly when an infectious process was present. The galactose tolerance test was within normal limits in all patients studied. There was a wide variation in the results recorded for the bromsulphalein dye test. There was a definite correlation between the level of the plasma prothrombin and the synthesis and excretion of hippuric acid following the ingestion of sodium benzoate as measured by the method of Quick. Confirmation at operation and necropsy has shown that these two tests are sensitive reflectors of hepatic damage. A relatively extensive degree of damage to the parenchymatous tissue of the liver must be present before it is reflected in many of the commonly used hepatic function tests. The ability of the liver to form prothrombin from vitamin K and to synthesize hippuric acid from sodium benzoate is a more sensitive measure of the amount of hepatic damage present than the majority of hepatic function tests would indicate. Prothrombin cannot be replaced by blood transfusion in sufficient quantity to be of any therapeutic value.

Kansas Medical Society Journal, Topeka

41:321-364 (Aug.) 1940

Treatment of Peptic Ulcer. W. L. Palmer, Chicago.—p. 321.
Value of Determination of Basal Metabolic Rate to the General Practitioner. W. H. Olmsted, St. Louis.—p. 325.
Erysipeloid: Report of Thirteen Cases Among Veterinary Students at Kansas State College. H. T. Gross, Manhattan.—p. 329.
*Appendicitis with Complete Situs Inversus Viscerum. C. W. Lawrence, Emporia.—p. 333.
Acute Ascending Paralysis (Landry's Paralysis). R. L. Drake, Wichita.—p. 335.
Cinchophen Poisoning. M. G. Berry, Kansas City, Mo.—p. 337.
Sacralization of Coccyx. H. G. Hadley, Washington, D. C.—p. 339.

Appendicitis with Complete Situs Inversus Viscerum.—Lawrence cites a case of appendix located on the left side with complete transposition of the thoracic and abdominal viscera, diagnosed by physical examination and confirmed by x-ray study, the electrocardiograph and at operation. This anomaly was first recorded in the seventeenth century, four cases being reported. Many cases are probably not diagnosed, as it is said to occur once in every 5,000 necropsies. Up to 1924, 270 cases had been reported. The anomaly occurs more often in males than in females. In many instances there is a dextrocardia while the other viscera are in their normal position. A complete situs inversus of the viscera is compatible with health and longevity

and except as an anatomic curiosity is important only to the embryologist, cardiologist and surgeon. However, a partial transposition is often troublesome as it may interfere with the function of some parts due to malposition in relation to other organs. A clinical picture of an abdominal lesion except as to location of pain and point of sensitivity should be a warning and the diagnosis should be cleared up by a fluoroscopic examination of the chest, a barium sulfate meal and an enema. The subject is of much importance in abdominal surgery for, as Pol pointed out, more than half of forty-six patients with left side appendix complained of pain in the right lower abdomen, referred pain. Usually pain produced by an irritated abdominal viscus is first referred to the epigastrium and later to the viscus involved or to the opposite side from the viscus involved. The electrocardiograph will clear up the diagnosis of a case of dextrocardia, as lead 1 will be inverted and leads 2 and 3 will be transposed. X-ray study is necessary in diagnosing transposition of the abdominal viscera. The author's patient was a girl of 19 who had been complaining of pain in the right lower part of the abdomen for twelve hours. She had a similar attack one year previously. The maximal cardiac impulse was found in the fifth intercostal space in the right side of the chest. There was rigidity in both the right and the left iliac fossa, but the patient insisted that the pain was mostly in the right side except on deep pressure, when it was more intense on the left. At operation a right rectus incision was made and the sigmoid was found in the right iliac fossa and the cecum in the left fossa. The appendix was delivered without much difficulty, the abdomen was closed and recovery was uneventful.

Medical Annals of District of Columbia, Washington

9:261-290 (Aug.) 1940

Some Remarks on Diagnosis and Treatment of Pulmonary Tuberculosis. J. N. Hayes, Saranac Lake, N. Y.—p. 261.
Chronic Otorrhea. J. N. Novick, Washington.—p. 267.
Hypertensive Heart Disease in White and Colored Women: Comparison of Necropsy Data in the District of Columbia. Thelma B. Dunn, Washington.—p. 271.
Rest and Protection Treatment of Anterior Poliomyelitis. M. C. Cobey, Washington.—p. 275.
General Principles of Laboratory Procedure in Cases Presenting Albuminuria. H. E. Ragle, Washington.—p. 277.

New York State Journal of Medicine, New York

40:1205-1274 (Aug. 15) 1940

Malignant Kidney Tumors: Study of Cases at the Rochester General Hospital During a Twelve Year Period. I. A. Gáspár, Rochester.—p. 1209.
Jaundice. H. G. Jacobi, New York.—p. 1218.
Operative Treatment of Cataract Other Than the Senile Type. T. LeWin, Buffalo.—p. 1228.
Streptococcic Pneumonia. E. A. Lawrence and W. D. Sutliff, New York.—p. 1233.
Agranulocytosis Forme Fruste. W. Pewny, Bratislava, Czechoslovakia.—p. 1236.
Epidemics of Diarrhea in the Newborn. W. D. Ludlum, Brooklyn.—p. 1238.
Rheumatic Heart Disease in Pregnant Women: Treatment in City Hospital. J. Clahr, M. D. Klein and N. M. Greenstein, New York.—p. 1242.
Treatment of Diabetes Mellitus in Patients in the Older Age Group. M. B. Handelsman and J. K. Bradford, Brooklyn.—p. 1248.

Ohio State Medical Journal, Columbus

36:817-920 (Aug.) 1940

Intestinal Obstruction in Newborn Due to Congenital Anomalies. D. M. Glover and C. A. Hamann, Cleveland.—p. 833.
Primary Sarcoma of Ileum with Perforation: Case Report. C. F. Frankman, Greenville, and D. H. Drummond, Brooklyn.—p. 841.
Use of Hormones in Cryptorchism. C. E. Zeithaml, Cleveland.—p. 843.
Adrenalin in Oil: Results When Used as Inhalation and Intratracheal Injection. A. E. Cohen, Louisville, Ky.—p. 846.
Dynamic Conception of Psychopathic Personality. M. Levine, Cincinnati.—p. 848.
Laryngotracheobronchial Obstructions and Their Secondary Effects. T. C. Galloway, Evanston, Ill.—p. 851.
Diabetes Mellitus. F. Anzinger Jr., Springfield.—p. 855.
Acute Surgical Diseases of Abdomen in Children. M. T. Hoerner, Dayton.—p. 859.
Infantile Paralysis. C. W. Burhans, Lakewood.—p. 865.
Pharmacologic Shock Therapy: Recent Studies Presented at the Meeting of the American Psychiatric Association. J. L. Fetterman, Cleveland.—p. 868.
Pyelonephritis: Case Presenting Clinical Problems. H. L. Rinehart, Columbus.—p. 870.

Oklahoma State Medical Assn. Journal, Oklahoma City

33:1-58 (Aug.) 1940

Local Treatment of Nasal Allergy. O. A. Watson, Oklahoma City.—p. 1.
Exstrophy of Bladder: Experimental and Clinical Study of Cases. G. H. Kimball and N. R. Drummond, Oklahoma City.—p. 2.
Diagnosis and Treatment of Malaria. W. L. Shippey, Poteau.—p. 8.
Treatment of Trachoma. J. H. Hammond, Tulsa.—p. 12.
Rheumatic Fever: Types, Diagnosis and Treatment. C. J. Roberts, Enid.—p. 15.
Tinea Capitis. J. B. Hix, Altus.—p. 18.

Pennsylvania Medical Journal, Harrisburg

43:1521-1664 (Aug.) 1940

*Nutritional Disturbances in Relation to Skin Diseases. G. C. Andrews, New York.—p. 1535.
Practical Aspects of Stereoscopic Roentgen Ray Pelvimetry: Report of 125 Cases. R. E. Tafel, Pittsburgh.—p. 1541.
Oxygen Therapy. P. A. Faix, Pittsburgh.—p. 1545.
Changing Trends in Treatment of Some Common Disorders of the Preschool-Age Child. Emily P. Bacon, Philadelphia.—p. 1549.
Problem of Multiple Pregnancy. J. C. Hirst, Philadelphia.—p. 1553.
Clinical Interpretation of Leukocytic Pictures. M. M. Strumia, Penn Valley.—p. 1556.
Perirenal and Perinephric Infections. C. N. Haines, Sayre.—p. 1561.
Carbuncle or Solitary Abscess of Kidney. W. L. Estes Jr., Bethlehem.—p. 1566.
Unusual Sites of Metastasis from Carcinoma of Rectum and Sigmoid Colon. H. E. Bacon, Philadelphia.—p. 1573.
Diabetes: IV. Education of the Diabetic Patient. Anna O. Stephens, Laurelton.—p. 1579.
Human Sterility: Analysis of Series of 400 Specimens of Spermatic Fluid. R. H. McClellan, Pittsburgh.—p. 1582.
Vertex Occipitoposterior Positions. R. A. D. Gillis, Pittsburgh.—p. 1586.
Field Changes in Intracranial Tumors. C. R. Heed, Philadelphia.—p. 1592.

Nutritional Disturbances and Cutaneous Diseases.—In addition to well recognized deficiency syndromes there are, according to Andrews, a variety of abnormal conditions of the skin and mucous membranes in which the vitamin B complex is an important factor. The action of nicotinic acid and riboflavin on oral lesions is sufficient to suggest its use more widely and perhaps as a routine prior to operation in cases in which other oral lesions are associated with carcinoma of the tongue or buccal cavity. Whereas the results of treatment are not absolutely conclusive there is a strong suggestion that certain cases of oral leukoplakia are manifestations of a deficiency of some fraction of the vitamin B complex. Also some cases of neurodermatitis may have a nutritional background, and photosensitization may in some cases be a manifestation of vitamin deficiency. There are thirty-six (Spies) known dietary constituents essential to adequate nutrition. Little is understood concerning the body's requirements for some of these factors, and even less is known of the interrelationship of these substances to metabolism. The diet is influenced by the age, race, habits, taste and economic status of the patient. In general, however, treatment of deficiency states should include a diversified diet of from 4,000 to 4,500 calories, be rich in meat, liver, eggs and milk, and be supplemented by dry brewers' yeast and some of the fish oils.

Rhode Island Medical Journal, Providence

23:129-144 (Aug.) 1940

Recent Concepts of Convulsive Disorders. C. P. Fitzpatrick, Howard.—p. 129.
Delirium as Danger Signal. I. C. Nichols, Providence.—p. 132.
Early Medical History of Kent County, Rhode Island: J. H. Eldredge, President of the Rhode Island Medical Society, 1858-1860. H. DeWolf, Providence.—p. 135.

South Carolina Medical Assn. Journal, Greenville

36:211-240 (Aug.) 1940

Modern Conception and Treatment of Prenatal Syphilis. J. J. Kane, Beaufort.—p. 211.
Injuries of Pleura and Lung. E. F. Parker, Charleston.—p. 219.
Male Climacteric. W. R. Mead and R. Stith, Florence.—p. 222.

Tennessee State Medical Assn. Journal, Nashville

33:289-332 (Aug.) 1940

Mode of Action of Sulfanilamide. M. T. Bush, Nashville.—p. 294.
Sulfanilamide and Its Compounds: Their Uses in Medicine. J. O. Manier, Nashville.—p. 296.
Sulfanilamide in Surgery. M. J. Tendler, Memphis.—p. 300.
Toxic Manifestations of Sulfanilamide and Allied Drugs. F. E. Marsh, Chattanooga.—p. 305.
Gastritis. J. Witherspoon, Nashville.—p. 309.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

48:469-536 (Aug.) 1940

*Appendicitis with Complications: Reduction in Mortality Due to Use of Continuous Gastrointestinal Decompression. R. Ward, San Francisco.—p. 469.
Tumors in Infants and Children: Conservative Surgical Therapy. C. W. Brunkow, Portland, Ore.—p. 480.
Management of Surgical Injuries to Ureter. A. B. Hepler, Seattle.—p. 486.
*Prostigmine in Treatment of Ureteral Stones. A. J. Scholl, Los Angeles.—p. 493.
Endometriosis of Umbilicus. H. S. Chapman, Stockton, Calif.—p. 496.
Carcinoma of Breast. A. A. Matthews, Spokane, Wash.—p. 502.
Team Work in the Care of the Surgical Patient. I. Wills and A. H. Elliot, Santa Barbara, Calif.—p. 508.
Traumatic False Saccular Aneurysm Resulting from Erosion of Femoral Artery in Patient with Hereditary Deforming Chondrodysplasia. E. Butler and M. W. Debenham, San Francisco.—p. 511.
Fecal Fistula Following Appendicitis: Report of Eighteen Hospital Cases and Nineteen Cases from Literature. A. N. Collins, Duluth, Minn.—p. 514.
*Thyroid Surgery in Cardiac Disease. J. deJ. Pemberton and J. M. Miller, Rochester, Minn.—p. 518.
Technical Problems in Surgical Management of Large Cervical and Intrathoracic Goiter. C. J. Hunt, Kansas City, Mo.—p. 524.

Appendicitis with Complications.—Ward points out that the reduction in mortality following continuous gastrointestinal decompression was not great but that it indicated ways of still further improving the results. At the University of California Hospital 206 patients with acute appendicitis were operated on from 1913 to 1925 and 561 from 1925 to 1939. During the latter period decompression was known, but unfortunately not always used. The reduction in mortality was from 5.8 to 3 per cent and an analysis of the causes of death suggests that transduodenal decompression was the most important factor in this reduction. In a group of seventy-two patients with gangrenous, not perforated, appendixes there were no deaths. In the cases in which perforation with local peritonitis had taken place the mortality was reduced from 14.3 per cent in the early period to 5 per cent in the later period. In perforation with diffuse peritonitis the mortality decreased from 40 per cent in the early period to 27.2 per cent in the later period. In cases of abscess in which drainage only was carried out there has been no change in the mortality rate, while for those in whom abscess was treated by drainage and appendectomy the mortality rate doubled. However, two of these deaths were probably unpreventable under any plan of treatment and if they are eliminated the mortality rate would be identical for the two periods. In 41 per cent of the deaths there was a history of the use of cathartics and more than half of the patients had been sick longer than four days before being sent to the hospital. The author believes that only five of the twenty-nine deaths could not have been prevented by any plan of management and that some change in handling might have eliminated twenty-four deaths. The plan of management that he suggests is as follows: 1. Operation for appendicitis should be performed when the diagnosis is made or strongly suspected, except in the presence of diffuse peritonitis, if rigidity has given way to flaccid distention or if the patient is moribund. Such patients are to be treated with immediate intestinal decompression by nasal tube, restoration of fluid and electrolytic balance, use of the Fowler position and morphine. 2. Under spinal anesthesia, or occasionally local anesthesia, reinforced by pentothal sodium or evipal soluble administered intravenously, the appendix should be approached through a gridiron incision over its suspected site and removed with the cautery under adequate exposure with continuous suction evacuation of pus or serous fluid and with a minimal disturbance of the surrounding structures. The stump should be closed by simple ligation or inversion without ligation if the cecal wall is not indurated and the abdominal cavity without drainage, unless a well walled-off abscess has been found. 3. The abdominal wall should be drained adequately in the infected cases or the wound packed with petrolatum gauze if greatly contaminated. 4. Postoperatively, intestinal decompression should be instituted without waiting for distention. Comfort and intestinal tone should be maintained by morphine, fluid and electrolytic balance according to the plan laid down by Coller, and fluids and food by mouth should be withheld until peristalsis has returned without the use of artificial stimulants. 5. An aerobic and anaerobic culture should be obtained at the time of operation for guidance in specific postoperative therapy. As a test of the plan the author says that in his last hundred personal cases in which he followed these rules there have been two deaths. Both patients were inmates of a home for the aged and their necropsy reports read like a catalogue of diseases of mankind and included everything from syphilis to coronary occlusion. Both had a gangrenous perforated appendix and he thinks that death was inevitable.

Prostigmine for Ureteral Stones.—Scholl suggests that one or two series of injections of prostigmine methylsulfate be given every patient with ureteral stones before any manipulative or surgical measures are instituted. He used the drug in fifteen personally observed cases, and in seven it was of definite help. In all except three cases, in which small stones were present in the lower ureter, some other procedure was also used; usually the passage of a soft ureteral catheter up to or by the stone in an effort to establish the diagnosis. In none of the fifteen cases were stone dislodgers, metal dilators or multiple catheters used. In the three cases with small stones, the stones were passed promptly after the first prostigmine injections. Hager's original recommendation of dosage is still the most satisfactory.

Thyroid Surgery in Cardiac Disease.—Pemberton and Miller believe that for a complete conception of cardiac physiology in relation to the hyperthyroid states the condition must be thought of in terms of altered, increased metabolism. A certain degree of cardiovascular disturbance is almost invariably associated with thyrotoxicosis. Thus in such cases the clinical signs related to the cardiovascular system are easily explicable on the basis of an increased circulatory rate. The latter is merely the result of the changes in the body economy dictated by an increased metabolic rate. The most common disorder of cardiac rhythm is auricular fibrillation. Its persistence following thyroidectomy is suggestive of the presence of associated primary cardiac disease, residual cardiac injury from protracted hyperthyroidism or recurrent hyperthyroidism of exophthalmic goiter. Most of these patients are prepared for operation in about two weeks and are not hospitalized unless congestive failure is present. Patients suffering from congestive heart failure should have rest and be treated for primary cardiac disease without hyperthyroidism. When compensation is attained the patient should be ambulatory in a limited fashion for several days. Debilitation from prolonged rest and the ravages of hyperthyroidism make him susceptible to postoperative pulmonary complications. This period of limited activity also affords a test of cardiac reserve. The most frequent accompanying cardiac disorders are coronary sclerosis and coronary and hypertensive cardiac disease. Cardiac disease as a complication accounts for approximately 81 per cent of the total mortality. However, even though the chances of recovery are slim the surgeon must remember that his estimate of risk is subject to error and that every patient should be given the opportunity to avoid the status of a "cardiac cripple." An analysis of the causes of death reveals that the primary cause was bronchopneumonia. This proves the value of establishing precautionary measures in the entire period of treatment to avoid respiratory infections. Attention should also be focused on atrophy of the liver. The relation of hepatic failure to surgical risk in cases of hyperthyroidism has not received sufficient consideration. Because of the high risk entailed, every possible precaution must be exercised and technical errors avoided in these cases. The choice of the anesthetic agent to be used is a prime consideration. Local infiltration supplemented by inhalation of nitrous oxide and oxygen has proved effective. Prolonged anesthesia by inhalation is avoided and the susceptibility to pulmonary complications is reduced. The average duration of inhalation anesthesia will be from eight to ten minutes. Local anesthesia, unsupplemented, is indicated for patients with obstructive dyspnea. The indications for lobectomy are limited. Patients in an extremely toxemic condition with limited reserve and patients with congestive heart failure may have to be subjected to lobectomy to minimize the hazard. Such patients need special preoperative and postoperative preparation. Such care is most effectively achieved by the internist and the surgeon as a team. The risk of operation for such individuals is great but when the great number of excellent results are reviewed it seems justified.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

24:373-420 (Aug.) 1940

Convergence Deficiency. Ida Mann.—p. 373.
*Specific Inflammation of Cornea in Chickenpox. A. Loewenstein.—p. 391.
Multiple Ruptures of Choroid with Retention of Good Vision. H. Neame.—p. 399.
Exfoliation of Lens Capsule with Pathologic Report: Case. A. Garrow and I. C. Michaelson.—p. 400.
Some Cases of Traumatic Myopia. O. G. Morgan.—p. 403.

Corneal Inflammation in Chickenpox.—Loewenstein reports two cases of iris disorder following chickenpox which is parallel to that seen in smallpox, in herpes iridis (herpes zoster), in inoculated herpes iridis in rabbits and in vaccinia. Depigmented spots of the iris remained after the exanthem healed. This, the author says, completes his earlier observation of vitiligo iridis following chickenpox. He believes that the now recognized forms of vitiligo iridis in smallpox, chickenpox, herpes iridis (zoster), inoculation iritis in rabbits (herpes febrilis) and scarlet fever present a unity from which a biologic relationship between their germs can be deduced. The corneal infection does not correspond with any known change of the cornea. It cannot be confused with anything else. The involvement of the deeper layers of the corneal parenchyma in the first weeks of the infection and their rising to the surface later on is striking. The concomitant iritis is a slight one. The slit lamp depicts only the tiny exudate on the lens capsule. No opacities in the fluid of the anterior chamber are detected and no new formation of vessels in the cornea. Photophobia is absent even toward the end of the inflammation when the surface layers (epithelium) are more involved. The author thinks that this observation is the long sought "missing link." On biologic grounds, being aware of the appearance of a vitiligo iridis in chickenpox, one expected to find the process causing the acute disease—a process which had previously escaped observation. As the assumed virus of chickenpox is related to the virus of herpes, it was to be expected that the clinical picture of chickenpox keratitis would be very similar to that of a deep herpes. This assumption proved to be true. He wonders how the disturbance escaped recognition with chickenpox being so widespread. He does not believe that the corneal involvement in chickenpox is a rare one, but since the majority of chickenpox cases heal without medical assistance and parents know that even the eye complications are not dangerous, ophthalmologists do not attend the patients and therefore the condition has apparently been missed.

British Journal of Radiology, London

13:257-292 (Aug.) 1940

Localization and Extraction of Radiopaque Objects by Means of "Light Compasses." C. Chaussé.—p. 257.
Effect of X-Rays on Tumor Growth When Tumor Itself Is Not Irradiated. S. Russ and G. M. Scott.—p. 267.
Two Unusual Gastrointestinal Cases. I. B. Barclay.—p. 273.
Effect of X-Rays on Cells Cultivated in Vitro. I. Lasnitzki.—p. 279.
Optimal Densities of Radiographs. G. E. Bell and E. E. Smith.—p. 285.
Gallbladder Visualized by Gas. P. Kerley.—p. 289.
Venous Thrombosis Following Injection of Uroselectan B. F. H. Kemp.—p. 291.

British Medical Journal, London

2:143-178 (Aug. 3) 1940

Vitamin C Requirements of Native Mine Laborers: Experimental Study. F. W. Fox, L. F. Dangerfield, S. F. Gottlich and E. Jokl.—p. 143.
Surgical Treatment of Air Raid Casualties: Review of Twelve Cases. A. R. Hodgson and G. K. McKee.—p. 147.
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Malignant Stomal Ulcer: Case. S. A. Yaffe.—p. 153.

2:179-212 (Aug. 10) 1940

*Pulmonary Embolism and Infarction. B. Parsons-Smith.—p. 179.
Muscular Rheumatism: Local Injection Treatment as Means of Rapid Restoration of Function. M. Button.—p. 183.
Chronic Blepharitis in Children: Its Treatment with Aniline Dye Compound. A. T. Elder.—p. 185.
Chronic Acetanilid Poisoning. T. N. Morgan and A. G. Anderson.—p. 187.
Tender Teeth: Their Surgical Importance. H. T. Roper-Hall and A. P. Bertwistle.—p. 188.

Pulmonary Embolism and Infarction.—According to Parsons-Smith, pulmonary embolism is a disability chiefly affecting people at or past middle life. A variety of factors are concerned in the formation of the thrombus from which the embolus originates. They include local trauma, the presence of organisms and several morbid developments such as slowing of the blood stream, chemical and physical changes in the blood and injury of the vascular epithelium. The primary thrombosis occurs often in the external iliac, the femoral or the saphenous veins; but other vessels—the inferior vena cava and the pulmonary and internal iliac veins—may be responsible, as also may the heart itself in the advanced stages of myocardial failure. The clinical picture of embolic obstruction of the main pulmonary artery or its major branches is moderately distinctive. Some of these cases are immediately fatal; in others characteristic signs and symptoms are observed for varying periods before death, the patient being suddenly seized with breathlessness, faintness and feelings of severe substernal oppression which tend to persist in spite of treatment. Physical examination discloses the shock syndrome. Characteristic signs include pallor, sweating, lividity and dilated pupils; the pulse is rapid and soft and the blood pressure considerably lowered; the respiratory rate is accelerated and its excursion usually diminished; collapse, often ushered in by uncontrollable vomiting, deepens, and unconsciousness generally preludes death. It may prove difficult to differentiate pulmonary embolism from coronary thrombosis, because during the early stages the two are singularly alike. The clinical phenomena common to both are pain in the chest, tachycardia, rapid respiration, pallor, cyanosis and a soft and frequently imperceptible pulse, a falling blood pressure, shock with syncopal tendencies, sweating, vomiting and cardiographic signs typical of myocardial ischemia. The past history of the patient and the circumstances leading up to the onset of the illness will often furnish details helpful in the differential diagnosis. Previous heart disease, an exhausting period of decompensation and the clinical phenomena suggestive of long-standing hypertension or a history of effort angina favor the development of coronary thrombosis. On the other hand, pulmonary embolism might be suspected if the acute seizure is a sequel to an operation or accident. Moreover, the pain of pulmonary embolism is usually referred to the side of the chest rather than to the substernal region. Other features peculiar to pulmonary embolism include extreme cyanosis and breathlessness associated with shallow respiration, the discomfort in the side being intensified by any attempt to increase the depth of the breathing. Apart from cases of massive embolization in which pulmonary edema occurs rather than hemorrhagic consolidation, the incidence of true infarction with moderate-sized emboli is relatively small. Chronic cardiac disease, postoperative invalidism and septic wounds seem to favor the formation of pulmonary infarcts, the responsible factor being passive hyperemia in the lungs. A slightly raised temperature and a relatively rapid pulse may be the only indications that a focus of phlebitis and venous thrombosis which may be responsible in due course for embolization in the pulmonary circuit and, later, for a hemorrhagic infarct, is in process of formation. As early indications of the latter, the temperature and the pulse rate rise abruptly, the respiration quickens, and the symptoms of shock and mental anxiety are intensified. Pain, exaggerated by deep breathing, is another early symptom. The physical signs of pulmonary infarction are rarely distinctive. A friction rub may be audible; there may be a circumscribed area of dulness with rales and altered breath sounds and diminished expansion on the side of the lesion. X-ray examination is often a valuable aid in the diagnosis. The clinical picture of pulmonary embolism and infarction should be supplemented by electrocardiographic investigation.

Lancet, London

2:155-184 (Aug. 10) 1940

*Capillary Fragility: Critical Analysis. G. H. Bell, S. Lazarus and H. N. Munro.—p. 155.
*Excretion of Pregnandiol in Toxemia of Pregnancy. C. L. Cope.—p. 158.
Reduction of Fractures of Forearm, Wrist and Metacarpals. T. M. J. d'Offay.—p. 159.
Mortality from Lobar Pneumonia in London. W. J. Martin.—p. 161.
Method of Arresting Clot in Transfusion with Stored Blood. A. M. Giles.—p. 162.
Lordosis and Muscular Dystrophy. G. E. Donovan.—p. 162.
Culture of Yellow Fever Virus in Vitro. G. M. Findlay and F. O. MacCallum.—p. 163.

Capillary Fragility.—Bell and his colleagues sought to determine the variations in the capillary fragility by Göthlin's test among 346 healthy British students, to define the range of normality and to determine the effect of ingested vitamin C on those students considered to have an increased capillary fragility. The number of small cutaneous hemorrhages occurring under standard conditions was taken as an index of the capillary fragility or resistance. Variations in the illumination altered the mean number of petechiae detected. A 300 watt lamp at a distance of 2 feet proved to be a good illuminating standard. Among 89.3 per cent of the students, less than eight petechiae were found. Under the conditions of the test eight or more petechiae may be regarded as unusual; this agrees with the opinion reached by Göthlin. The ingestion of vitamin C by the thirty-five students who had a petechial count of eight or more reduced the petechial count to less than eight in two weeks. The ingestion of vitamin C had no effect on petechial counts of less than eight. The antecubital fossa was found to be as suitable as the forearm for the test. There were five healthy persons among the 346 whose increased capillary fragility was not influenced by the administration of vitamin C or of vitamin P. This, the authors believe, is the only reported group of healthy people with an increased capillary fragility resistant to treatment with vitamin C in whom the effect of vitamin P has been studied. Apart from abnormal influences—for example fever and the administration of heavy metals—two factors influence capillary fragility in health: menstruation and ascorbic acid. Other factors may be involved, as in the few students whose high petechial counts were unaffected by the administration of vitamin C or any other factor so far known. The authors found that even when the conditions were carefully standardized it still remained difficult to assess the capillary fragility of the subject. Variation in the values found on the right and left arms of a single individual were frequent. Therefore they suggest that the average of the petechial count on the two arms of an individual appears to give a more accurate indication of the true capillary fragility. Göthlin now makes all determinations on both arms and proceeds from the mean figure of the two determinations.

Excretion of Pregnandiol in Toxemia of Pregnancy.—Cope states that observations on ten pregnant women suffering from toxemia uncomplicated by nephritis have not confirmed the claim that the amount of the sterol complex pregnandiol glucuronidate excretion, which is abundant in the urine in normal pregnancy, is greatly reduced in late toxemia of pregnancy. Pregnandiol was, however, absent in the last week of pregnancy from the urine of a pregnant woman with chronic nephritis. This suggests to the author that renal damage may be a more likely cause of interference with the excretion of pregnandiol. He considers it unwise to conclude that any difference which may be found between the rates of excretion of pregnandiol in normal pregnancies and in pregnancy toxemia is necessarily due to the toxemia, for the excretion of pregnandiol might be interfered with by many conditions of ill health other than toxemia. He has compared the daily excretion of pregnandiol glucuronidate in late pregnancy toxemia with that of women having other general diseases late in pregnancy. The patients with pregnancy toxemia not only had a persistent albuminuria but also a raised blood pressure with or without edema, and one woman had severe eclamptic fits. The study shows that in none of these cases was the daily excretion low (from 28.5 to 55.8 mg.): the mean daily excretion was 39.4 mg. The excretion among the ten pregnant women with other diseases (hypochromic anemia, cardiac failure, diabetes mellitus, pyelitis and others) were much more variable; the mean value, 49.5 mg. a day, was essentially the same as in normal pregnancies. It was rather higher than the mean of the toxemic group, but the difference does not seem large enough to be of significance.

South African Medical Journal, Cape Town

14:251-270 (July 13) 1940

Doctors' Hobbies: Music and the Gramophone. N. V. Storr.—p. 253.
"Robert Knox and His South African Research." P. R. Kirby.—p. 254.
Diet and Osteodystrophic Diseases in Domestic Animals. A. I. Malan.—p. 261.

Bull. of Health Org., League of Nations, Geneva

8:551-796 (Nos. 4-5) 1939

Tuberculosis in Rural Areas. G. Ichok.—p. 551.
Organization of Public Health in Rural Areas of Belgium. R. Sand.—p. 617.
Public Health Organization of Province of Luxemburg. M. Graffar.—p. 640.
Application of Health Indexes Selected for Rural Districts to Providence of Luxemburg (Belgium). M. W. Selleslags.—p. 649.
Recent Trend of Medicosocial Policy in Europe. R. H. Hazemann.—p. 662.
Report of the Housing Commission.—p. 732.

Schweizerische medizinische Wochenschrift, Basel

70:661-684 (July 13) 1940

Hydrochloric Acid Collargol Reaction. W. Nagel.—p. 661.
Chemotherapy with Sulfamethylthiazole. A. Fischer.—p. 666.
Cranial Traumatism and Craniocerebral Wounds Caused by Projectiles. A. Jentzer.—p. 667.
*War Injuries of the Thorax. T. Naegeli.—p. 674.
*Diseases of Coronary Vessels and Military Service. M. Holzmann.—p. 676.

War Injuries of the Thorax.—Naegeli points out that the prognosis in cases of bilateral pneumothorax is grave. In unilateral open thoracic wounds a displacement of the mediastinum toward the uninjured side occurs with decreased ventilation of the uninjured lung and unsatisfactory blood arterialization as a consequence. In gaping intercostal soft part wounds the collapsed lung may eventually be pressed out of the thoracic wound by means of compressed breathing enabling thus the wound to close, or else the retracted lung may be fixed by lying on the wounded side or by percutaneous suture. Even closing of the thoracic wound with airtight dressing or suturing soft parts improves the patient's condition, as the injurious variations in pressure during breathing become thereby eliminated. The consequences of valvular and tension pneumothorax are tympanites over the lungs, widening of the intercostal spaces, cyanosis and dyspnea. It is treated by puncture, preferably with a cannula provided with a valve toward the outside. Severe phenomena of displacement due to hemorrhage following injury of a lung vessel also require puncture. A small blood transfusion favors arrest of the hemorrhage. The mediastinal emphysema requires an incision into the suprasternal fossa. In pleural empyemas, puncturing and suction should be used. Change of dressing should possibly be done without getting air into it. In view of possible infection, large and particularly torn soft wounds of the thoracic wall should be excised and eventually sutured. Morphine should be amply administered during the first days. The patients may be best transported in a sitting position leaning on the injured side. Severely wounded patients or patients who have been operated on should not be transported for twenty days at least.

Coronary Vessel Disease and Military Service.—Holzmann states that in diseases of the coronary vessels the main clinical symptom is angina pectoris. Three types may be distinguished: 1. The effort-angina of fifteen minutes duration at the most, caused by a transient and reversible coronary insufficiency. 2. Increased attacks of angina that may occur at rest and may last longer than fifteen minutes, caused by increased and protracted coronary insufficiency. They are reversible, although they leave behind a lasting ischemic injury to the myocardium. 3. The status anginosus of greatest intensity, caused by an acute irreversible coronary occlusion with a massive infarction of the heart as a consequence. It often occurs without provocation and lasts from hours to days. Gradually

and imperceptibly developing coronary stenosis is at the bottom of the first two forms. Thrombotic occlusion of the small coronary arterial branches may occur in the second form. An acute thrombosis of an important coronary arterial branch occurs in the third form. Besides the degree of impassibility of the diseased vessels, the ability of accommodation of the collateral circulation is significant. Anginal pains are not necessarily caused by disease of the coronary vessels. They may also be produced by a transient functional disturbance, as in case of angina pectoris vasomotoria or in the initial stages of tobacco angina. They may be the consequence of a relative coronary insufficiency, as in case of hypertrophic hearts. The angina pectoris ambulatoria is typically localized, radiating into the left shoulder, left arm or both arms. It lasts a few minutes and is influenced by physical effort, whence the diagnostic value of carefully dosed physical labor. A glyceryl trinitrate tablet dissolved in the mouth may also demonstrate the ischemic nature of the ailment by its quick sedative effect. In status anginosus of greatest intensity the pain can be allayed only with morphine or its substitutes. In the presence of a coronary circulatory disturbance the army physician should hospitalize the patient for further examination. This consists in taking electrocardiograms at rest and in case of negative observations after physical labor. Fluoroscopy of the thorax, blood pressure, sedimentation and Wassermann reactions complete the examination. Should this disclose a lesion of the myocardium or a coronary insufficiency, the patient should be kept under observation and treatment until the symptoms have disappeared or a stationary condition has been obtained. The following situations may arise before the military examining commission: 1. No more anginous symptoms, heart physically normal, electrocardiogram normal, no heart insufficiency: dispensation from service for three months. In case the physical condition remained satisfactory after a trial period in service following the dispensation period: fit for auxiliary service, armed eventually. 2. Anginous symptoms still present or electrocardiogram shows pathologic condition, eventually both, physically unnoticeable or slightly abnormal heart condition, no heart insufficiency: administrative auxiliary service at most. 3. Presence of heart insufficiency, electrocardiogram reveals pathologic condition, whether angina pectoris is present or not and whether physical heart condition is abnormal or not: unfit for service. Estimation of military insurance liability remains subjective. Refusal of claim is justified only when symptoms occurred without strenuous physical labor and infectious or toxic influences in service, provided prompt medical measures were taken. The safest estimate can be made in case of death and necropsy.

Archivos Argentinos de Pediatría, Buenos Aires

13:557-665 (June) 1940. **Partial Index**

Lymphosarcoma of Mediastinum. A. Casaubon, J. L. Monserrat and A. Letamendi.—p. 557.
*Sulfanilamide in Treatment of Erysipelas in Children. F. Bazán and R. Maggi.—p. 593.

Sulfanilamide in Erysipelas in Children.—Bazán and Maggi used sulfanilamide in the treatment of acute erysipelas of the head and face or the limbs of thirty children ranging in age from 2 to 10 years. The disease developed in the majority of cases in the course of convalescence from scarlet fever, diphtheria or chickenpox. The drug was given by mouth in daily doses which varied between 0.1 and 0.15 Gm. for each kilogram of body weight, in three or four fractional doses, up to forty-eight hours after the return of the temperature to normal, after which half the dose was given for two or three more days. The treatment as a rule lasted from five to eight days. All the patients recovered. Improvement was noted on the first day of treatment by the arrest of the spread of the lesion and a diminution of inflammation, redness and local tension. The authors found that the height of fever and the course of the disease were favorably influenced by sulfanilamide and that the duration of both diminished when compared with the effects of previous therapeutic methods. They conclude that sulfanilamide is the treatment of choice in erysipelas of children, since the treatment is well tolerated and yields a recovery in 100 per cent of the cases. The drug appears to have a specific effect on the streptococcus and on the disease itself.

Vrachebnoe Delo, Kharkov

22:161-240 (No. 3) 1940. **Partial Index**

Sanitation and Medical Service in Western Ukraine and in White Russia in the Past and Today. D. V. Gorfin.—p. 165.
Hepatopancreatorenal Syndromes. A. I. Frankfurt.—p. 173.
Catarrhal Jaundice and Serous Inflammation of Liver. A. S. Berlyand and P. I. Lirtsman.—p. 177.
*Treatment of Parenchymatous Jaundice. A. Firdman.—p. 179.
Jaundice on the Basis of Gastrogenous Hepatitis. M. M. Pismarev and M. S. Kiveliovich.—p. 183.
Alimentary Chloridemia in Diseases of the Liver. L. S. Lifshits and E. V. Kosevich.—p. 185.

Treatment of Parenchymatous Jaundice.—In his clinical observations on thirty-six cases of jaundice, Firdman noted a positive urobilin reaction in the course of the disease indicating the presence of a hepatitis. Fractions of bile from the duodenal contents revealed cloudiness in fractions A and C, leukocytes, cylindric epithelium and mucus on microscopic examination. Toward the termination of the disease the duodenal bile became clear and transparent. The patients were treated by intravenous injection of from 3 to 4 cc. of a 40 per cent solution of methenamine and from 16 to 17 cc. of a 40 per cent solution of dextrose. The injections were given daily or every other day. Patients received a milk diet, an occasional mild laxative and a warm bath every other day. Gastric intubation was practiced several times in the course of the disease. The average hospital stay amounted to 20.3 days. There were no instances of transition to acute yellow atrophy, despite the fact that some of the cases were severe and exhibited in the beginning symptoms suggestive of impending acute yellow atrophy. The author concludes that the combined methenamine and dextrose treatment is capable of shortening the course of parenchymatous jaundice and of preventing its passage into acute yellow atrophy.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:1727-1772 (July 16) 1940

*Clinical Investigations in Connection with Beriberi: So-Called Subclinical Vitamin B_1 Deficiency. F. M. Meyers.—p. 1727.
Determination of Protein Content of Blood of Patients with Nutritional Edema. A. G. van Veen.—p. 1747.
Some Diseases of Bones of Foot. S. A. Tahar.—p. 1761.
Leproid Skin Eruptions in Frambesia. M. Soetopo.—p. 1765.

Subclinical Vitamin B_1 Deficiency.—Meyers points out that in the temperate zones the subclinical deficiencies of vitamin B_1 show a much wider range of symptoms than do those of the tropics. He thinks that this is due to the fact that, in the Netherland East Indies at least, B_1 deficiencies are relatively uncomplicated and chiefly of exogenous origin, whereas in European countries and in the United States these subclinical deficiencies are often caused by alcoholism and chronic diseases of the intestinal tract and are complicated by an atypical form of pellagra. The author investigated the vitamin B_1 excretion in the urine of fourteen healthy Javanese laborers before and after the subcutaneous administration of vitamin B_1. Attention was paid also to the diuretic effect of vitamin B_1 and to its influence on the increase in blood pressure after epinephrine. The results of these investigations could be compared with observations on three healthy "prepared" persons who had received a diet with a high vitamin B_1 content and on three patients with beriberi. The daily excretion of vitamin B_1 in the healthy laborers varied between 0 and 63 micrograms. After the injection the excretion varied between 2 and 50 per cent (in most cases between 10 and 30 per cent). One of the three healthy "prepared" persons showed excretion values of the same order as did the patients with beriberi. In nine of the fourteen laborers the administration of vitamin B_1 had a diuretic effect. However, there was no clear correlation with the vitamin B_1 excretion values. This vitamin has the properties of a true diuretic. In three of eight healthy persons the increase in systolic blood pressure after epinephrine became much stronger after vitamin B_1 had been administered. The same was observed in the patients with beriberi but in none of the three "prepared" persons. Thus this vascular reaction proved to be helpful in determining deficiency of vitamin B_1 where other means had failed; but no correlation could be detected with the excretion of vitamin B_1 in the urine. The excretion of vitamin B_1 in the urine by itself often does not produce figures sufficiently unequivocal to judge whether deficiency exists or not.